IMPROVING the Diagnosis & Treatment of GENERALIZED ANXIETY DISORDER:

A Dialogue Between Mental Health Professionals and Primary Care Physicians

ADAA
Sponsored by the Anxiety Disorders Association of America

IMPROVING the **Diagnosis & Treatment** of GENERALIZED ANXIETY DISORDER:

A Dialogue Between Mental Health Professionals and Primary Care Physicians

AD AA

Sponsored by the
Anxiety Disorders Association of America

Supported by an unrestricted
educational grant from Pfizer Inc

CONTENTS

ADAA GAD ROUNDTABLE PARTICIPANTS

Jonathan Abramowitz, PhD
Mayo Clinic
Rochester, Minnesota

Kathryn Connor, MD
Duke University
Durham, North Carolina

Larry Culpepper, MD, MPH
Boston University
Boston, Massachusetts

Brian Doyle, MD
Georgetown University Medical Center
Washington, DC

Lynn Epstein, MD
Brown University
Providence, Rhode Island

Jack M. Gorman, MD
Mount Sinai School of Medicine
New York, New York

Rudolf Hoehn-Saric, MD
Johns Hopkins Medical School
Baltimore, Maryland

Eric Hollander, MD
Mount Sinai School of Medicine
New York, New York

Gregory Leskin, PhD
National Center for PTSD
VA Palo Alto Health Care System
Menlo Park, California

Thomas McGinn, MD
Mount Sinai Medical Center
New York, New York

Jan Mohlman, PhD
Syracuse University
Syracuse, New York

Philip Ninan, MD
Emory University School of Medicine
Atlanta, Georgia

Bruce Rollman, MD
University of Pittsburgh
Pittsburgh, Pennsylvania

Jerilyn Ross, MA, LICSW
President and CEO, ADAA
Director, The Ross Center for Anxiety and Related Disorders
Washington, DC

Martin Seif, PhD
Private Practice
New York, New York

M. Katherine Shear, MD
University of Pittsburgh
Pittsburgh, Pennsylvania

Jeff Susman, MD
University of Cincinnati
Cincinnati, Ohio

Risa Weisberg, PhD
Brown University
Providence, Rhode Island

Sally Winston, PsyD
The Anxiety and Stress Disorders Institute
Towson, Maryland

OBJECTIVES

On January 13, 2004, in Washington, DC, the Anxiety Disorders Association of America (ADAA) convened a roundtable meeting with leaders in mental health and primary care. The purpose of this program was to harness the collective knowledge and experiences of these clinicians and researchers in discussions about the diagnosis and treatment of generalized anxiety disorder (GAD) and make recommendations for improvements that could be applied within the context of primary health care.

Following a presentation by Risa Weisberg, PhD, on the results of the Primary Care Anxiety Project (PCAP), the essential information needs of primary care were assessed by the entire group, both collectively and within breakout sessions. This publication presents the outcomes of this meeting and provides practical information on managing patients with GAD. The critical points identified by the group include the impact of GAD; the presentation of GAD symptoms; the need for screening tools; barriers to treatment; initial management strategies; treatment selection; and improving the communication between the patient, primary care physician, and mental health professional.

INTRODUCTION

Anxiety disorders are the most common psychiatric illnesses affecting both children and adults, with an estimated 19 million adult Americans suffering from anxiety disorders. Anxiety disorders may develop from a complex set of risk factors, including genetics, brain chemistry, personality, and life events. The ADAA categorizes these disorders as GAD, obsessive-compulsive disorder (OCD), panic disorder, posttraumatic stress disorder (PTSD), social anxiety disorder, and phobias. Anxiety disorders are highly treatable with psychosocial therapies, medication, or both, yet only about one-third of those suffering from an anxiety disorder receive treatment.

GAD is a chronic, persistent, and disabling condition that is associated with significant use of health care resources in primary care. Patients with GAD are characterized by excessive, unrealistic worry that lasts six months or more; in adults, the anxiety may focus on issues such as health, money, career, timeliness, repairs, or the security of their children. For most anxious patients, their anxiety produces a degree of suffering that is underestimated by outside observers. Since most people have regular contact with primary health services, patients with GAD are likely to see their family physician even though their psychological problem may not be the reason for the consultation. The challenge to primary care physicians (PCPs) is to identify those patients with GAD that require treatment and to select appropriate therapy.

In addition to chronic worry and irritability, physical symptoms of GAD include trembling, muscular aches, insomnia, abdominal upsets, and dizziness. Also, the patient with GAD often has poor psychosocial functioning, has somatic symptoms that have no identifiable physiologic foundation, and may have health anxiety or hypochondriasis. GAD is highly comorbid with other medical and psychiatric disorders and increases the risk and severity of these disorders. The chronic nature of GAD often contributes to its lack of recognition as a treatable disorder, both by the patient and the PCP. Treatment patterns in primary care are often symptom-specific interventions rather than GAD-specific interventions. Increased recognition, early intervention, and appropriate treatment will facilitate recovery and reduce rates of relapse.

PREVALENCE, OUTCOMES, AND UNIQUE ASPECTS OF GAD

Lifetime prevalence estimates for GAD are thought to be 5% according to the *Diagnositc and Statistical Manual of Mental Disorders,* Fourth Edition (DSM-IV), and 6.5% according to European ICD-10 criteria.[1] Current prevalence is likely to range from 2%-3% of the general population, yet GAD remains poorly recognized and poorly treated. More than half of patients with an anxiety disorder receive treatment from a primary care provider.[2] Among patients seen by PCPs, GAD has an 8% prevalence rate, making GAD the most prevalent anxiety disorder in the primary care setting (Figure 1).[3]

FIGURE 1: POINT PREVALENCE OF SYMPTOMS AND DSM-IV DIAGNOSES OF GAD IN PRIMARY CARE (N = 17,739 PATIENTS)

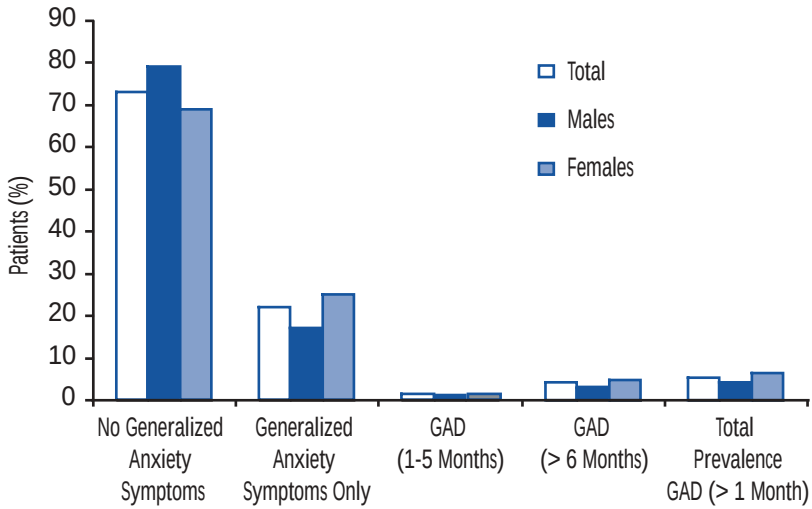


Figure 1: Point prevalence of DSM-IV GAD in primary care (N = 17,739 patients). 558 physicians participated in the Generalized Anxiety and Depression in Primary Care study (GAD-P). Symptoms and diagnosis of generalized anxiety were assessed using the Generalized Anxiety Screening Questionnaire, a modified version of the Anxiety Screening Questionnaire.[3]

The clinical course of GAD is chronic, episodic, and fluctuating in severity. To launch the dialogue among participants at the ADAA GAD Roundtable, Risa Weisberg, PhD, presented a prospective, naturalistic, longitudinal, multicenter study of 539 primary care patients with anxiety disorders (PCAP) that examined the course of GAD over 4 years (Figure 2). Low rates of recovery from GAD (48%) were observed over the course of the study.[4]

FIGURE 2: FOUR-YEAR COURSE OF GAD IN PCAP

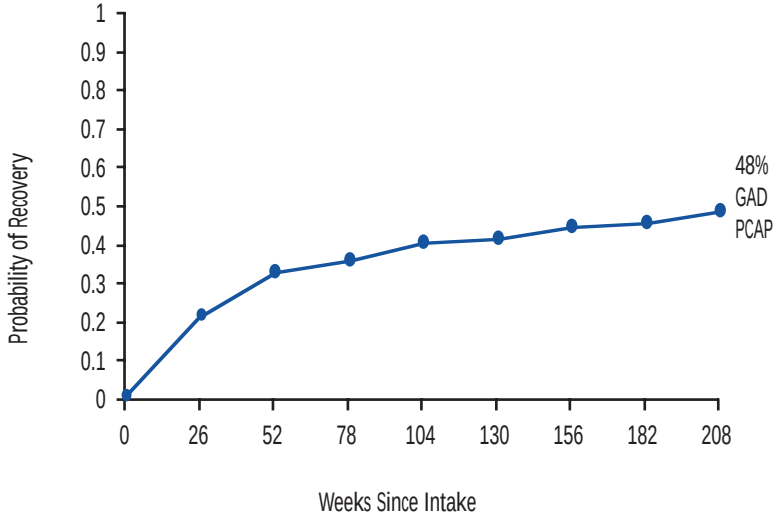


Figure 2: The cumulative probability of recovery was examined in the PCAP, a prospective, naturalistic, longitudinal, multicenter study of 539 primary care patients with anxiety disorders. Recovery was defined as 8 consecutive weeks with almost no symptoms of the disorder (PSR 1 or 2). The data for years 3 and 4 are still preliminary as this is an ongoing study.[4]

In this study, participants were less likely to recover from GAD with a younger age of GAD onset or with ongoing or lifetime nonpsychiatric medical conditions. Patients with comorbid GAD and major depressive disorder (MDD) had increased risk of suicidality and perceptions of impoverished physical and psychosocial functioning, both compared with the general population. Despite significant levels of impairment in functioning, a large proportion of the GAD patients were not receiving mental health treatment. Many who were not receiving treatment cited the lack of a doctor's recommendation and concerns about treatment itself, including side effects and not believing in the treatment.

Because GAD symptoms do not follow a consistent pattern and may fluctuate over time, long-term management of the disorder is often necessary. When GAD is the patient's primary psychiatric disorder, the age at onset may be as early as 13 years; when GAD develops secondary to another anxiety disorder, age of onset may be as late as 30 years. Females are affected twice as often as men.[5] GAD has a relatively low rate of recovery when recovery is defined as a reduction to only 1 or 2

symptoms with a subjective sense of returning to normal. Using this definition, GAD has a 20% rate of recovery, while MDD has an 80% rate of recovery.[6] GAD has a high rate of recurrence.

A very high rate of comorbidity exists between anxiety disorders, such as panic disorder, and MDD.[7,8] Roughly 58% of patients suffering from lifetime MDD will have some form of anxiety disorder. Depression is a "more acceptable diagnosis" and is often considered a medical condition. Anxiety disorders generally present earlier, in childhood, and present with more somatic symptoms. Patients with GAD and depressive disorders are generally more severely ill than patients with GAD alone and have poorer prognoses.[9]

Studies investigating the etiology of GAD have focused on the role of catecholamines; autonomic reactivity; and the serotonin, γ-butyric acid (GABA), and cholescystokinin neurotransmitter systems. The current effective pharmacological treatments for GAD all modify serotonergic, noradrenergic, or GABAergic systems, while future therapies will probably interact with other, novel systems.

DETECTION AND DIAGNOSIS OF GAD

The PCP plays a significant role in initial screening and diagnosis of GAD (Table 1). Some of the challenges to detection of GAD by PCPs are the DSM-IV terminology (Table 2), patient resistance to diagnostic test procedures, translating the symptoms into a diagnosis, and eliminating organic possibilities. There is a critical need for valid, time-efficient screening and monitoring systems for all anxiety disorders.

TABLE 1. PATIENT HISTORY[10]

- In patients presenting with somatic or psychological complaints consistent with an anxiety disorder, ask about anxiety-related symptoms, their duration, and the nature of the patient's worries.
- Especially in patients presenting with general, nonspecific, or vague somatic complaints, consider the possibility of an anxiety disorder and ask specifically about psychological concerns, including the psychological symptoms of tension, worry, and nervousness.
- When asking questions about the past medical history and review of systems, consider possible medical causes of anxiety, including reactions to medications. Ask about the use of sedative-hypnotic or antianxiety medications as well as alcohol usage.
- Inquire about the specific symptoms of each anxiety disorder, and consider the possibility that panic attacks may coexist with GAD.
- Ask detailed questions about psychosocial stressors, especially if they have a temporal relationship to the patient's symptoms.
- Ask if there is any family history of anxiety or mood disorders.
- Ask about the patient's responses to symptoms and about strategies used to alleviate symptoms.
- In patients who appear functionally impaired secondary to a mental or physical disorder, consider the use of a self-administered questionnaire to assess the degree of impairment.

The core presenting complaints of primary care patients with GAD rarely provide clear clues for correct diagnostic decisions since GAD usually presents as a multiplicity of disorders. The PCP is faced with the challenge of differentiating GAD from medical conditions and concurrently differentiating GAD from other psychiatric conditions. The high rate of comorbidity (90% in primary care) reflects that the PCP will have to identify when GAD is present in addition to MDD or another anxiety disorder.

As many as 83% of patients initially present to their PCP with general, vague, or nonspecific somatic complaints, such as pain syndromes, symptoms of autonomic arousal (chest pain, palpitations, hyperventilation), headache, fatigue, insomnia, and gastrointestinal symptoms.[11] A psychiatric presentation (17% of patients) occurs when the patient self-diagnoses a specific disorder. In the Generalized Anxiety and Depression in Primary Care Study of 558 primary care practices, Wittchen and coworkers found that 87% of patients with GAD do not present with anxiety as their primary symptom.[3] High utilizers present with a myriad of complaints not typically observed in other patients and display behavioral predictors including frequent visits with many expensive tests (treadmill testing, thallium scans, endoscopy, arteriograms, and pulmonary function tests) and no ensuing diagnosis.

Primary care patients can also present with an accepted reason for their somatic symptoms of anxiety.[12] In many of these cases, GAD patients may consider their anxiety an inherited personality trait, and their PCPs label them as worriers, failing to recognize the underlying anxiety disorder. In the elderly, concomitant psychiatric or somatic illnesses are problematic because symptoms of anxiety may be mixed with symptoms of depression, physical illness, and cognitive impairment.[13]

TABLE 2. DSM-IV CRITERIA FOR GAD[14]

- For more than half the days in at least 6 months, the patient experiences excessive anxiety and worry about several events or activities
- The person has trouble controlling these feelings
- Associated with this anxiety and worry, the patient has 3 or more of the following symptoms, some of which are present for over half the days in the past 6 months:
  - Feels restless, edgy, keyed up
  - Tires easily
  - Trouble concentrating, tendency for the mind to go blank
  - Irritability
  - Increased muscle tension
  - Trouble sleeping (initial insomnia or restless, unsatisfying sleep)
- The symptoms cause clinically important distress or impair work, social, or personal functioning
- The disorder is not directly caused by a general medical condition (eg, hyperthyroidism) or by substance abuse, including medications and drugs of abuse
- Anxiety and apprehension is not associated only with a mood disorder, psychotic disorder, PTSD, or pervasive developmental disorder

The differential diagnosis of GAD is complex and includes medication side effects and substance-related dependence or withdrawal phenomena as well as endocrine, neurologic, cardiorespiratory, and autoimmune disorders. Risk factors for anxiety disorder include a family history of anxiety disorder or alcoholism, history of depression or anxiety disorder, age younger than 40 years at onset of the anxiety-related symptoms, and history of alcohol abuse. GAD should be considered if the patient is starting an antidepressant, has a history of substance abuse, or shows a high demand and urgent need for care as indicated by repeated office or ER visits with negative work-ups. Diagnoses suggestive of an anxiety disorder include atypical chest pain, hyperventilation, and irritable bowel syndrome.

Many medical conditions can be masked by symptoms of anxiety, including chronic obstructive pulmonary disease, coronary insufficiency, hypoparathyroidism, pancreatic tumor, pheochromocytoma, some epilepsies, pulmonary emboli, and some presentations of coronary artery disease. In contrast, medication for an acute or chronic medical condition can cause anxiety symptoms. Even with the patient who presents with only somatic complaints, it is important to ask specifically about psychological concerns, including psychosocial stressors and the psychological symptoms of tension, worry, and nervousness. The patient may not have considered or identified their symptoms as anxiety.

MANAGEMENT OF GAD

GAD can be treated with pharmacotherapy, psychotherapy, or both. Treatment selection is dependent on numerous factors, including the patient characteristics and preference, previous response to treatment, accessibility to each approach, short-term *versus* long-term goals, patterns of comorbidity, medical issues (eg, pregnancy), sensitivity to side effects, skills of the clinician, relative costs, and the availability of resources. The short-term goals of the treatment of GAD include a reduction of somatic symptoms, relief from psychic stress such as overwhelming worry, and resolution of symptoms such as insomnia. Long-term goals in the treatment of GAD are full recovery, the prevention of relapse or recurrence, and relief from any comorbid disorders such as depression.

Pharmacotherapy (eg, antidepressants or benzodiazepines) and psychotherapy (eg, cognitive behavioral therapy [CBT]) have been shown to be efficacious in GAD. In CBT, the person gradually learns to see situations and problems in a different perspective and learns the methods and techniques to use to alleviate and reduce anxiety. The main drawback to psychological therapy is its limited availability, since few physicians are trained in providing this type of treatment, particularly in rural areas. Combining pharmacotherapy (antidepressants and/or benzodiazepines) and psychotherapy may lead to an increase in improvement in patients not responding to one treatment approach alone. Before initiating treatment, the patient should be educated about both pharmacological and psychological approaches, and a determination should be made of treatment preference and motivation. General lifestyle measures include exercising regularly, obtaining adequate amounts of sleep, and avoiding caffeine and alcohol.

Pharmacological Treatment of GAD

The main goal of pharmacotherapy in GAD is to rapidly treat the chronic worry and tension with agents that have few adverse effects and limited potential for abuse. These agents are taken on a long-term basis since early discontinuation of pharmacotherapy is highly likely to lead to relapse.

Side effects of medications such as sexual dysfunction and weight gain may play a role in treatment choices. In patients with a comorbid chronic medical illness, the potential for drug-drug interactions exists and must be evaluated. Anxiolytic agents, such as benzodiazepines and buspirone, and antidepressants, such as tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), trazodone, and nefazodone have all been shown to be effective in the treatment of GAD (Table 3).

TABLE 3. PHARMACOTHERAPY IN GAD[15]

Anxiolytics

- Benzodiazepines
  - *Alprazolam (Xanax®)*
  - *Chlordiazepoxide (Librium®)*
  - *Clonazepam (Klonopin®)*
  - *Chlorazepate (Tranxene®)*
  - *Diazepam (Valium®)*
  - *Lorazepam (Ativan®)*
  - *Oxazepam (Serax®)*
- Buspirone (BuSpar®)

Antidepressants

- SSRIs
  - *Citalopram (Celexa®)*
  - *Escitalopram (Lexapro®)**
  - *Fluoxetine (Prozac®)*
  - *Fluvoxamine (Luvox®)*
  - *Paroxetine (Paxil®)**
  - *Sertraline (Zoloft)*
- SNRI
  - *Venlafaxine (Effexor®)**
- TCAs
  - *Clomipramine (Anafranil®)*
  - *Desipramine (Norpamin®)*
  - *Imipramine (Tofranil®)*
  - *Nortriptyline (Aventyl®)*
- Heterocyclic Antidepressants
  - *Nefazodone (Serzone®)*
  - *Trazodone (Desyrel®)*

**These products are approved by the FDA for the treatment of GAD.*

Antidepressants may worsen or aggravate anxiety upon initiation due to their side effects; therefore treatment must be initiated at low doses, and consideration should be given to adding short-term benzodiazepine therapy due to their faster onset of therapeutic effects. Benzodiazepines are thought to be useful for acute somatic symptoms, while antidepressants are thought to improve long-term psychic symptoms.[16]

Anxiolytics

Benzodiazepines: alprazolam (Xanax®), chlordiazepoxide (Librium®), clonazepam (Klonopin®), clorazepate (Tranxene®), diazepam (Valium®), lorazepam (Ativan®), oxazepam (Serax®)

Benzodiazepines are often used for short-term, initial treatment of GAD and have sometimes been used for longer-term maintenance of GAD. The mechanism of anxiolytic action of the benzodiazepines is to increase the affinity of $GABA_A$ receptors for GABA (γ-aminobutyric acid), a major inhibitory neurotransmitter in the brain. While benzodiazepines have a rapid onset of action and low cost, they also carry a risk of dependency. Several additional factors limit the utility of benzodiazepines, including adverse events such as sedation, fatigue, impaired psychomotor performance, decreased learning ability, synergistic effects with alcohol, and the potential for abuse. With maintenance therapy, however, some of these negative effects may become transient or disappear.

The chronic nature of GAD encourages long-term treatment. The use of benzodiazepines for several weeks leads to physical tolerance and physical and psychological dependence in some patients. Discontinuation of treatment with benzodiazepines can be followed by relapse, rebound anxiety, and withdrawal symptoms; rapid withdrawal increases the risk of seizures. A very slow tapering schedule over a prolonged period of time is often required to avoid such symptoms. Withdrawal symptoms are believed to occur with greater frequency and severity with prolonged use, abrupt discontinuation, and with rapidly eliminated benzodiazepines.

Buspirone (Buspar®)

Buspirone is a 5-HT_{1A}-receptor partial agonist that has mild efficacy combined with a delayed onset of anxiolytic action of 2-3 weeks. It has a short half-life and therefore must be taken several times a day. Buspirone does not potentiate the effects of alcohol and produces less drowsiness than other antidepressants and no psychological dependence. Buspirone is rarely used as monotherapy in primary care, however, because it is not effective for the comorbidities associated with GAD (MDD and other anxiety disorders).

Antidepressants

Many antidepressants such as imipramine, venlafaxine, and several of the SSRIs have demonstrated therapeutic efficacy in treating the symptoms of GAD at doses similar to those used for treating major depression.[17] Bupropion (Wellbutrin®, Zyban®), an antidepressant of the aminoketone class, is indicated for the treatment of depression but is not effective for anxiety disorders.

TCAs: clomipramine (Anafranil®), desipramine (Norpamin®), imipramine (Tofranil®), nortriptyline (Aventyl®)

The first antidepressants used for GAD were the TCAs at doses similar to those for major depression. TCAs reduce reuptake of serotonin or norepinephrine or both and have a slow onset (2-3 weeks). The numerous anticholinergic side effects, cardiovascular risks, and dangerous overdose potential limit their utility.

Heterocyclic Antidepressants: nefazodone (Serzone®), trazodone (Desyrel®)

Trazodone is an antidepressant with efficacy comparable to the TCAs and benzodiazepines for acute GAD but with a better safety profile. Trazodone's mechanism of action is not clear, but it has been shown to inhibit serotonin reuptake and may have effects on other receptors as well. Nefazodone is a 5-HT_2 receptor antagonist that has been reported to inhibit the reuptake of serotonin and norepinephrine (not, however, at clinicallly-relevant doses).[18,19]

SSRIs: citalopram (Celexa®), escitalopram (Lexapro®), fluoxetine (Prozac®), fluvoxamine (Luvox®), paroxetine (Paxil®), sertraline (Zoloft®)

The SSRIs have benefits in major depression and some have clinical indications for use in GAD and other anxiety disorders such as panic disorder, OCD, PTSD, and social phobia. Disadvantages to SSRIs include the need for dose titration due to initial side effects of increased anxiety, slow onset of anxiolytic action, and adverse effects including sexual dysfunction and weight gain. Other common side effects of SSRIs are gastrointestinal (especially nausea) and neuropsychiatric (particularly headache and tremor), although several of these resolve after the first weeks of therapy. The abrupt discontinuation of some of the SSRIs can cause a withdrawal reaction characterized in some people by dizziness, vertigo, light headedness, nausea, and parethesia. Differences exist between the SSRIs in effects on specific cytochrome P450 enzymes resulting in drug-drug interactions. Monitoring may be useful in the elderly, poor metabolizers, and patients with liver or renal impairment.

SNRI: venlafaxine (Effexor®)

Venlafaxine inhibits reuptake of serotonin and norepinephrine. Venlafaxine is indicated for acute and long-term treatment of GAD and is effective in treating depression and depressive symptoms in patients with GAD. Venlafaxine is available in an extended-release form. The side effects of venlafaxine are similar to those of the SSRIs. In addition, there is a small risk of reversible elevation of blood pressure.

Future Therapeutic Approaches

Future therapeutic approaches in the treatment of GAD include agents that modify cholecystokinin (CCK), neurokinins (NK), serotonin 5-HT_{1A} receptors, γ-aminobutyric acid (GABA), and voltage sensitive Ca^{2+} channels (Table 4). Neuroactive peptide (such as CCK and NK) antagonists are under investigation in the treatment of anxiety disorders. CCK is an important neurotransmitter found in

the gut and in the brain, and it may interact with other neuronal systems in anxiety. The CCK_B receptor is commonly found in the central nervous system. NK (NK_1 and NK_2) receptor antagonists have been identified and investigated in rodent models of anxiety. Since the introduction of buspirone, research has been directed toward developing efficacious 5-HT_{1A} receptor agonists. GABA receptor modulators act at or near the $GABA_A$ receptor and have properties similar to benzodiazepines. Another promising treatment for GAD is pregabalin, which binds with high selectivity and affinity to the $\alpha_2\delta$ subunit of voltage-dependent Ca^{2+} channels in the brain and spinal cord. Pregabalin modulates, but does not block, the flow of Ca^{2+} channels in abnormally hyperexcited neurons.[20]

TABLE 4. FUTURE PHARMACOLOGICAL APPROACHES IN THE TREATMENT OF GAD

Neuroactive Peptides
- Cholecystokinin (CCK) receptor antagonists
- Neurokinin (NK) receptor antagonists

5-HT_{1A}-Receptor Agonists
- Flesinoxan
- Eptapirone

α_2-δ Voltage-Dependent Ca^{2+} Channel Ligand
- Pregabalin

$GABA_A$-Receptor Modulator
- Suriclone

5-$HT_{2A/2C}$ Antagonist
- Deramciclane

Psychotherapeutic Treatment of GAD

CBT is a type of psychotherapy that attempts to change the thoughts and behaviors that are fundamental to maintaining the anxiety disorder and includes exposure and cognitive restructuring (Table 5). CBT involves training the patient to detect internal and external stimuli that trigger anxiety and to apply newly learned coping skills that target the psychic and somatic symptoms of the disorder.[21,22] CBT is an interactive therapy, which is most effective with well-motivated patients. CBT has been shown to be efficacious in GAD.[23,24] For patients who choose CBT, the PCP can help in therapist selection. The patient must agree to the therapy for it to be effective. Few primary care patients with GAD actually receive CBT because of reimbursement policies, time, availability, and accessibility. An awareness of the principles of CBT by the PCP can be useful in counseling patients with GAD, especially in high utilizers of health care resources or those patients suffering from acute exacerbations. Supportive psychotherapy can be offered in the primary care setting including support, education/explanation, empathic listening, meaningful reassurance, encouragement, and guidance.

TABLE 5. CHARACTERISTICS AND BASIS OF MOST COGNITIVE-BEHAVIORAL THERAPIES[25]

- Based on the Cognitive Model of Emotional Response
  - Thoughts cause our feelings and behaviors, not external things, like people, situations, and events
- Time-limited and highly instructional in nature
  - The average number of sessions clients receive (across all types of problems) is only 16
- Therapists focus on teaching rational self-counseling skills
- Collaborative effort between the therapist and the client
- Based on stoic philosophy
  - Undesirable situations exist whether we are upset about them or not, therefore, at worst, patients learn to feel *calm* when confronted with undesirable situations
- Uses the Socratic Method
  - Cognitive-behavioral therapists often ask questions to gain understanding of a client's concerns
- Structure is present, with specific techniques/concepts taught during each session
- Based on an educational model
  - The scientific assumption that most emotional and behavioral reactions are learned and, therefore, the goal of therapy is to help clients *unlearn* their unwanted reactions and to learn a new way of reacting
- Relies on the Inductive Method
  - Encourages us to look at our thoughts as hypotheses that can be questioned and tested
- Homework is a central feature of CBT

Integrating Pharmacotherapy and Psychotherapy

CBT is highly compatible with pharmacotherapy and may be combined with pharmacotherapy, either concurrently, sequentially (CBT following initial symptom control), or to facilitate medication discontinuation. In many collaborative care programs, pharmacotherapy is coupled with CBT, with intensive management of adherence by a care manager. Integrating pharmacotherapy and psychotherapy may be useful in patients who can't take a full dose of medication or are afraid of medication in general. In treating patients with GAD, PCPs often act as providers for pharmacotherapy but almost always function as referrers for psychotherapy. This difference may become apparent and problematic if a patient has negative perceptions of psychotherapy (too time-consuming or doesn't believe in therapy) but is accepting of pharmacotherapy.

Monitoring the Progress of Treatment

A standardized scale for measuring the key features (eg, physical manifestations, worry, avoidance, etc) of GAD has not been validated in the primary care setting. The ADAA offers a GAD Self-Test on its Web site (see page 22) to help physicians and patients recognize the signs of GAD. In addition, questionnaires such as the Prime-MD may help identify patients with depressive and anxiety disorders. Symptom improvement during treatment can be monitored with the depression module of the Patient Health Questionnaire (PHQ-9)[26] in patients with comorbid depression. Patient progress can also be monitored by monthly or bimonthly office visits as well as patient documentation of symptom frequency and duration, situational triggers, and coping mechanisms utilized. Indications for referral to a mental health professional such as a psychiatrist, psychologist, or social worker are based on patient preference, severity, risk of self-harm, aggressive or homicidal thoughts, psychosis, suicidality, and the presence of substance abuse. In turn, a critical conclusion of the ADAA GAD Roundtable was that the PCP and mental health provider should follow up with one another and work as a team to facilitate the progress of treatment.

PATIENT EDUCATION IN GAD

Considering that avoidance behavior and worry are characteristics of GAD, it would be beneficial to present GAD as an exogenous disorder so it is not perceived as a rejection. To further help an individual accept both the diagnosis and its treatment, it is desirable for the physician to establish a comfortable relationship with the patient, maintaining open communication lines (Table 6). A candid physician-patient discussion should take place about how medication and/or psychotherapy treatment goals fit into the overall restoration of health and quality of life. When psychiatric therapy is considered an effective treatment option for a GAD patient, provide referrals to a mental health professional who specializes in CBT.

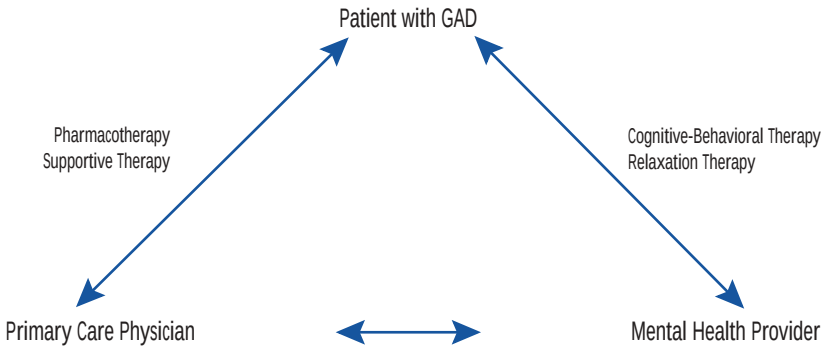
TABLE 6. PHYSICIAN COMMUNICATION WITH PATIENTS WITH GAD

- Describe the disorder as a treatable medical condition and that it may “run in families”
- Give supportive lifestyle counseling (avoiding caffeine, nicotine, and alcohol, managing insomnia, coping with daily stresses, exercise, proper diet)
- Provide an overview of the treatment options, goals, and side effects
- Indicate the need for follow-up treatment to feel better and continued monitoring for early signs of recurrence or relapse
- Describe the vulnerability to other disorders
- Encourage patients to keep a log of symptoms, medications, and lifestyle modifications
- When feasible, refer patients to an anxiety disorders “specialist”
- Keep reference materials in your office on self-help literature and Web sites for the patients to learn more about GAD

IMPROVING THE DIALOGUE AMONG THE PATIENT WITH GAD, THE PRIMARY CARE PHYSICIAN, AND THE MENTAL HEALTH PROFESSIONAL

To promote positive outcomes in GAD, primary care teams can educate patients about the treatment options and establish a system of referrals to anxiety disorders "specialists" for CBT. For patients with severe symptoms, PCPs may prescribe and monitor early pharmacotherapy in coordination with a CBT specialist. Long term, primary care teams can play an important role by following patients with GAD and by assisting them to initiate and maintain treatment to recovery. The ongoing care of the anxiety patient by the primary care team may be most effective if it is cooperative, including feedback (early side effects, response to treatment) and follow-up (titration, dosage adjustments, addition of psychotherapy) for long-term adherence to the treatment (Figure 3). Collaborative care is being investigated in patients with anxiety disorders and comorbid conditions seeking treatment through primary care providers. Collaborative care has been shown to improve outcomes for patients with depression in primary care systems[26]. Treatment is provided by a PCP, psychiatrist, and mental health specialist.

FIGURE 3. A MODEL OF COOPERATIVE CARE IN GAD



SUMMARY

To conclude the day of discussion during the ADAA GAD Roundtable, the participants reviewed the key points that were uncovered and recommended some next steps to move closer to improving the diagnosis and treatment of GAD.

Underrecognition of GAD in primary care occurs because of physician knowledge gaps, insurance regulations, time pressures, symptom attribution, perceptions of psychiatric disorders, the natural history of GAD, the diagnostic criteria applied, and frequent comorbidity.[11] The diagnosis of GAD can be further complicated by concomitant psychiatric or somatic illnesses, such as depression or other anxiety disorders. Medical conditions that evoke anxiety symptoms, such as hyperthyroidism, substance withdrawal, and cardiac arrhythmias or other organ system dysfunction, may reveal a cause of anxiety. It is possible for physicians to gain training in dual-diagnosis, and perhaps it would be beneficial to develop anxiety disorder curricula for use at the residency stage.

Management choices for GAD include pharmacotherapy (benzodiazepines and/or antidepressants), psychotherapy (CBT), or a combination of the two. Effective pharmacotherapy is dependent on proper dosing and duration of treatment as well as monitoring side effects. CBT includes examining irrational thoughts, learning to control worries, learning effective coping skills, and relaxation training, all of which may be incorporated on a basic level into the routine physician-patient discourse. Physicians and patients may also benefit from understanding the differentiation between therapies and a system of feedback.

Further education of physicians, health management organizations, and patients is the next step, ideally in a framework that decreases the workload of the PCP while maximizing the recovery of the patient. Much may be learned from the advances that have been made in the diagnosis and treatment of depression. Perhaps in today's technological environment, there are opportunities for electronic dissemination of materials. Subsequent to this Roundtable, the ADAA is organizing a conference on collaboration between primary care and the mental health profession to improve the care of people with anxiety disorders.

GAD and all other anxiety disorders are treatable medical conditions, like diabetes, and improving outcomes in patients with these disorders would have a positive impact on occupational functioning, health, service utilization, morbidity, and mortality.

RESULTS OF THE ADAA SELF-HELP SURVEY

The ADAA conducted an online survey (via www.adaa.org) to assess the use of self-help tools. Over a 4-week period from mid-February to mid-March 2004, 1100 individuals responded to the survey. Participants ranged in age from 18 to 82 years; > 50% of the respondents were younger than 35 years of age. Other demographics indicated a population that was 75% female and 85% Caucasian, with 60% of respondents indicating that they have immediate family members that have been treated for anxiety, depression, or other mental health concerns. Information gathered from this survey is consistent with the points made earlier in this publication about the importance of GAD to health care and its comorbidity with other mental health concerns, particularly depression and panic disorder (Figure 4).

FIGURE 4. SURVEY RESPONDENTS GIVEN A DIAGNOSIS FOR A MENTAL HEALTH CONCERN

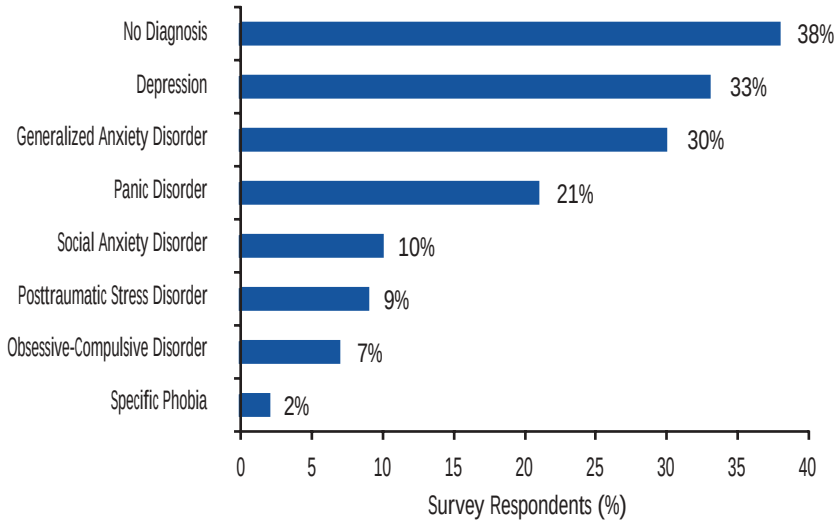


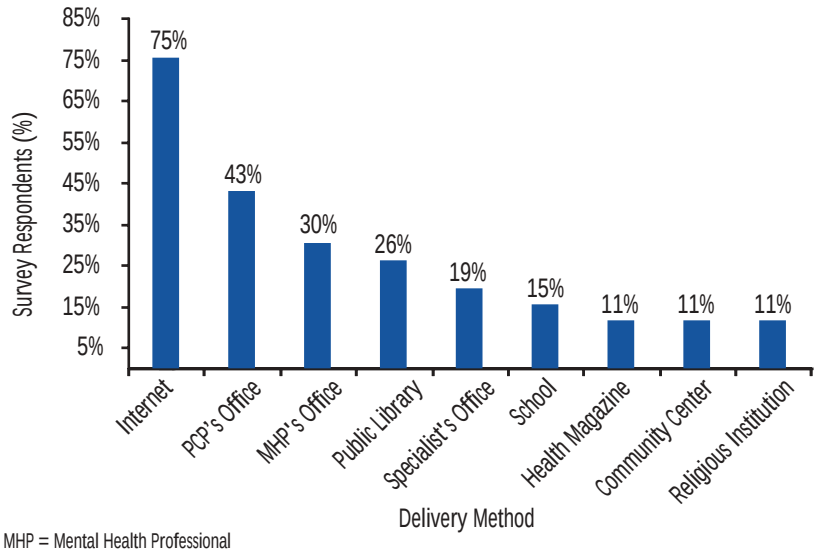
Figure 4. Percentage of individuals from the ADAA online self-help survey given a diagnosis by a health care professional, in the past 12 months, for a mental health concern.

Regarding the use of self-help tests during the past 12 months, 30% of participants took such tests mainly to address an anxiety-related problem on their own or to decide if they should seek professional help. Yet less than 50% of those respondents answered that they sought professional help within

6 months of taking a self-help test. Of the 770 respondents that have gone to a health professional for the treatment of an anxiety disorder or mental health problem, 35% visited a PCP. Those patients who received treatment for anxiety, depression, stress, nervousness, or lack of sleep were 3 times more likely to receive prescription medication than cognitive, behavioral, or exposure therapy.

When asked what would facilitate their use of self-help tools, 85% indicated that self-help tests should provide a score to indicate risk for a specific mental health disorder or the likelihood of a diagnosis for a specific disorder. For health care professionals looking for better ways to get important information to their patients, Figure 5 illustrates the preferred means of access to self-help tools.

FIGURE 5. PREFERRED MEANS OF ACCESS TO SELF-HELP TOOLS



MHP = Mental Health Professional

Figure 5. Preferred means of access to self-help tools as reported by participants in the ADAA online self-help survey.

SOURCES OF FURTHER INFORMATION

Anxiety Disorders Association of America
8730 Georgia Avenue, Suite 600
Silver Spring, MD 20910
Phone (240) 485-1001
Fax (240) 485-1035
http://www.adaa.org

American Psychiatric Association
1000 Wilson Boulevard, Suite 1825
Arlington, VA 22209-3901
Phone (703) 907-7300
http://www.psych.org/public_info/anxiety.cfm

American Psychological Association
750 First Street, NE
Washington, DC 2002-4242
Phone (800) 374-2721
http://www.apa.org

Association for Advancement of Behavior Therapy
305 7th Avenue, 16th Floor
New York, NY 10001
Phone (212) 647-1890
Fax (212)647-1865
http://www.aabt.org

The National Association of Cognitive-Behavioral Therapists
102 Gilson Avenue
PO Box 2195
Weirton, WV 26062
Phone (800) 853-1135
Fax (304) 723-3982
http://www.nacbt.org

National Institutes of Mental Health
The Anxiety Disorders Education Program
6001 Executive Boulevard
Room 8184, MSC 9663
Bethesda, MD 20892-9663
Phone (866) 615-NIMH (6464)
Fax (301) 443-4279
http://www.nimh.nih.gov/anxiety/anxietymenu.cfm

REFERENCES

1. Wittchen HU, Hoyer J. Generalized anxiety disorder: nature and course. *J Clin Psychiatry.* 2001;62(suppl 11):15-19.

2. Harman JS, Rollman BL, Hanusa BH, Lenze EJ, Shear MK. Physician office visits of adults for anxiety disorders in the United States, 1985-1998. *J Gen Intern Med.* 2002;17:165-172.

3. Wittchen HU, Kessler RC, Beesdo K, Krause P, Hofler M, Hoyer J. Generalized anxiety and depression in primary care: prevalence, recognition, and management. *J Clin Psychiatry.* 2002;63(suppl 8):24-34.

4. Bruce S et al. Management of anxiety disorders in primary care: implications for psychiatrists. Presented at: 156th Annual Meeting of the American Psychiatric Association; May 17-22, 2003, San Francisco, Calif.

5. Kessler RC, McGonagle KA, Zhao S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: results from the National Comorbidity Study. *Arch Gen Psychiatry.* 1994;51:8-19.

6. Keller MB. The long-term clinical course of generalized anxiety disorder. *J Clin Psychiatry.* 2002;63(suppl 8):11-16.

7. Scherrer JF, True WR, Xian H, et al. Evidence for genetic influences common and specific to symptoms of general anxiety and panic. *J Affect Disord.* 2000;57:25-35.

8. Gorman JM, Hirschfeld RM, Ninan PT. New developments in the neurobiological basis of anxiety disorders. *Psychopharmacol Bull.* 2002;36(suppl 2):49-67.

9. Gaynes BN, Magruder KM, Burns BJ, Wagner HR, Yarnall KS, Broadhead WE. Does a coexisting anxiety disorder predict persistence of depressive illness in primary care patients with major depression? *Gen Hosp Psychiatry.* 1999;21:158-167.

10. Rynn M, Scherrer MA, True WR. Generalized anxiety disorder (GAD). *Best Practice of Medicine.* November 2000. Available at: http://merck.praxis.md/index.asp?page=bpm_brief&article_id=BPM01PS07&hilight=rynn. Accessed April 7, 2004.

11. Culpepper L. Generalized anxiety disorder in primary care: emerging issues in management and treatment. *J Clin Psychiatry.* 2002;63(suppl 8):35-42.

12. Kessler D, Lloyd K, Lewis G, Gray DP. Cross sectional study of symptom attribution and recognition of depression and anxiety in primary care. *BMJ.* 1999;318:436-439.

13. Wetherell JL, Le Roux H, Gatz M. DSM-IV criteria for generalized anxiety disorder in older adults: distinguishing the worried from the well. *Psychol Aging.* 2003;18:622-627.

14. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders,* Fourth Edition, Text Revision. Washington, DC: American Psychiatric Association; 2000.

15. *Physician's Desk Reference.* 58th ed. Montvale, NJ: Thomson PDR; 2004.

16. Brawman-Mintzer O, Lydiard RB, Crawford MM, et al. Somatic symptoms in generalized anxiety disorder with and without comorbid psychiatric disorders. *Am J Psychiatry.* 1994;151:930-932.

17. Kapczinski F, Lima MS, Souza JS, Schmitt R. Antidepressants for generalized anxiety disorder (Cochrane Review). *Cochrane Database Syst Rev.* 2003;(2):CD003592.

18. Rickels K, Downing R, Schweizer E, Hassman H. Antidepressants for the treatment of generalized anxiety disorder. A placebo-controlled comparison of imipramine, trazodone, and diazepam. *Arch Gen Psychiatry.* 1993;50:884-895.

19. Cyr M, Brown CS. Nefazodone: its place among antidepressants. *Ann Pharmacother.* 1996;30:1006-1012.

20. Rickels K, Rynn M. Pharmacotherapy of generalized anxiety disorder. *J Clin Psychiatry. 2002;63(suppl 14):9-16.*

21. Falsetti SA, Davis J. The nonpharmacologic treatment of generalized anxiety disorder. *Psychiatr Clin North Am.* 2001;24:99-117.

22. Borkovec TD, Ruscio AM. Psychotherapy for generalized anxiety disorder. *J Clin Psychiatry.* 2001;62(suppl 11):37-42.

23. Borkovec TD, Costello E. Efficacy of applied relaxation and cognitive-behavioral therapy in the treatment of generalized anxiety disorder. *J Consult Clin Psychol.* 1993;61:611-619.

24. Butler G, Fennell M, Robson P, Gelder M. Comparison of behavior therapy and cognitive behavior therapy in the treatment of generalized anxiety disorder. *J Consult Clin Psychol.* 1991;59:167-175.

25. The National Association of Cognitive-Behavioral Therapists. What is CBT? Available at: http://www.nacbt.org. Accessed April 7, 2004.

26. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med.* 2001;16:606-613.

ADDITIONAL RESOURCES

Katon WJ. The Institute of Medicine "Chasm" report: implications for depression collaborative care models. *Gen Hosp Psychiatry.* 2003;25:222-229.

Leaman TL. Anxiety Disorders. *Prim Care.* 1999;26:197-210.

Michelini S, Cassano GB, Frare F, Perugi G. Long-term use of benzodiazepines: tolerance, dependence and clinical problems in anxiety and mood disorders. *Pharmacopsychiatry.* 1996:29:127-134.

Rauch SL, Rosenbaum JF. Approach to the patient with anxiety. In: Goroll AH, My L, Mulley AG, eds. *Primary Care Medicine: Office Evaluation and Management of the Adult Patient.* 3rd ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 1995:1022-1032.

Rickels K. Presented at: 155th Annual Meeting of the American Psychiatric Association; May 18-23, 2002; Philadelphia, Pa.

Roy-Byrne PP, Katon W. Generalized anxiety disorder in primary care: the precursor/modifier pathway to increased health care utilization. *J Clin Psychiatry.* 1997;58(suppl 3):34-38.

Sartorius N, Ustun TB, Lecrubier Y, Wittchen HU. Depression comorbid with anxiety: results from the WHO study on psychological disorders in primary health care. *Br J Psychiatry Suppl.* 1996;168:38-43.

Sinha SS, Gorman JM. Anxiety disorders. *Curr Pract Med.* 1999;2:873-880.

Spitzer RL, Williams JB, Kroenke K, et al. Utility of a new procedure for diagnosing mental disorders in primary care: the Prime-MD 1000 study. *JAMA.* 1994;272:1749-1756.

Sramek JJ, Zarotsky V, Cutler NR. Generalised anxiety disorder: treatment options. *Drugs.* 2002;62:1635-1648.

Tonks A. Treating generalised anxiety disorder. *BMJ.* 2003;326:700-702.

Wittchen HU, Zhao S, Kessler RC, Eaton WW. DSM-III-R generalized anxiety disorder in the National Comorbidity Survey. *Arch Gen Psychiatry.* 1994;51:355-64.

ADAA MISSION

Founded in 1980, the ADAA is the only national, nonprofit membership organization dedicated to informing the public, health care professionals, educators, and legislators that anxiety disorders are real, serious, and treatable. The ADAA promotes the early diagnosis, treatment, and cure of anxiety disorders and is committed to improving the lives of the people who suffer from them.

A volunteer Board of Directors governs the ADAA. Its members include clinicians who treat anxiety disorders and researchers who study these disorders as well as individuals who suffer from anxiety disorders and their families. Through individual and corporate contributions and membership dues, the ADAA is able to provide educational information and resources on anxiety disorders to those in need.

Through various activities, the ADAA aims to:

- Promote professional and public awareness of anxiety disorders and their impact on people's lives;
- Encourage the advancement of scientific knowledge about causes and treatment of anxiety disorders;
- Offer career development and research awards to develop a cadre of professionals focused on anxiety disorders research;
- Link people who need treatment with appropriate health care providers;
- Assist individuals with anxiety disorders in developing self-help skills; and
- Advocate for cost-effective treatment.

In recent years, the ADAA has been active in many public education campaigns, including improving the recognition and management of GAD in the primary care setting. The ADAA is one of four member organizations that founded the PTSD Alliance to provide educational resources to individuals diagnosed with PTSD and their loved ones; those at risk for developing PTSD; and medical, health care, and other front-line professionals. In 2003, the ADAA launched a Women's Initiative focusing on the need for diagnosis and treatment of anxiety disorders among women, who are twice as likely as men to suffer from an anxiety disorder.

The ADAA will be celebrating its 25th anniversary. In recognition of this milestone, the 25th Annual Conference will strive to clarify the relationship between anxiety disorders and other medical conditions and to describe and understand their impact on special populations. The annual conference covers panic disorder, GAD, OCD, social anxiety disorder, PTSD, and phobias. It will be held in Seattle, Washington, from March 17-20, 2005.

ADAA BOARD OF DIRECTORS 2004

HONORARY MEMBERS

ADAA GAD SELF-TEST

How much anxiety is too much? If you suspect that you might suffer from generalized anxiety disorder, complete the following self-test by checking the "yes" or "no" boxes next to each question and show the results to your health care professional.

HOW CAN I TELL IF IT'S GAD?

Are you troubled by:	Yes	No
Excessive worry, occurring more days than not, for a least six months?	○	○
Unreasonable worry about a number of events or activities, such as work or school and/or health?	○	○
The inability to control the worry?	○	○
Are you bothered by a least three of the following?		
Restlessness, feeling keyed-up or on edge?	○	○
Being easily tired?	○	○
Problems concentrating?	○	○
Irritability?	○	○
Muscle tension?	○	○
Trouble falling asleep or staying asleep, or restless and unsatisfying sleep?	○	○
Does your anxiety interfere with your daily life?	○	○

Having more than one illness at the same time can make it difficult to diagnose and treat the different conditions. Illnesses that sometimes complicate anxiety disorders include depression and substance abuse. With this in mind, please take a minute to answer the following questions

Have you experienced changes in sleeping or eating habits?	○	○
More days than not, do you feel:		
Sad or depressed?	○	○
Disinterested in life?	○	○
Worthless or guilty?	○	○
During the last year, has the use of alcohol or drugs:		
Resulted in your failure to fulfill responsibilities with work, school, or family?	○	○
Placed you in a dangerous situation, such as driving a car under the influence?	○	○
Gotten you arrested?	○	○
Continued despite causing problems for you and/or your loved ones	○	○

Reference
American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders,* Fourth Edition. Washington, DC: American Psychiatric Association; 1994.

Self-Test available at: http://www.adaa.org/public/index.cfm

For additional information please contact the ADAA at:

Anxiety Disorders Association of America
8730 Georgia Avenue
Suite 600
Silver Spring, Maryland 20910
Phone (240) 485-1001
Fax (240) 485-1035
Web site: www.adaa.org

Supported by an unrestricted educational grant from Pfizer Inc