Generalized Anxiety Disorder in Primary Care: Emerging Issues in Management and Treatment

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Generalized anxiety disorder (GAD) is highly prevalent in primary care patients and is a source of major morbidity. The low rate of recognition and diagnosis of GAD is often the result of insufficient knowledge on the part of primary care physicians, time pressures, and competing demands during patients' visits. Patient attribution of symptoms and the stigma related to mental illness also contribute to underrecognition. Other contributing factors include the natural history of GAD, the bimodal age of presentation, a chronic but waxing and waning course, frequent comorbidity with other anxiety and depressive disorders, and the controversy regarding the best diagnostic criteria. However, proper diagnosis is critical to appropriate management. Primary care management of GAD and associated comorbidities includes education about the nature of GAD as a medical disorder that is amenable to treatment and counseling about treatment alternatives and coping strategies. Most patients with GAD suffer from insomnia, and treating insomnia can be of great benefit to them. While cognitive-behavioral therapy and relaxation therapy are effective in treating GAD, most patients in primary care settings are likely to require pharmacologic treatment. Although commonly used, benzodiazepines and their short-term benefits are overshadowed by their decreased long-term effectiveness, their minimal treatment of psychic symptoms, and their degradation of patient performance. The selective serotonin reuptake inhibitor (SSRI) paroxetine is indicated for the short-term treatment of GAD, although adequate data supporting the use of most SSRIs for GAD are not yet available. The serotonin-norepinephrine reuptake inhibitor venlafaxine provides a treatment option resulting in both short- and long-term improvement of symptoms, attaining not only a response but also remission from GAD and prevention of relapse.

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The primary care physician manages the anxieties of numerous patients who have reached their limit in coping and turn to professional help with concerns about potential illness, pain, or other physical symptoms. The tension and stress associated with such concerns, particularly when unceasing, often leads to chronic activation of neuroendocrine systems that, in turn, exacerbate such symptoms through the sympathetic and parasympathetic systems.

The challenge for the primary care physician is to uncover the underlying causes and make an accurate diagnosis as a step toward helping the patient. For some patients, tension and stress at presentation have an uncomplicated physical cause. However, for other patients presenting with these symptoms, the true source of the problem is an anxiety disorder, particularly generalized anxiety disorder (GAD), which is often comorbid with other anxiety or depressive disorders.

Recognition of GAD is the first step in helping such patients. It requires familiarity with the manner in which patients present, the natural history of GAD, and the comorbidities often associated with the disorder. Once recognized, effective management requires the education of patients and their families, counseling for commonly associated symptoms such as insomnia and stress, and provision of treatment. For sustained improvement, treatment requires the use of effective agents, at an appropriate dose, continued until full recovery is attained. Recovery implies not only the absence of symptoms but also full resumption of functional roles, including family, social, and work-related roles. A final task for the physician is that of preventing relapse, and early recognition and treatment if relapse does occur. This article considers the diagnosis, management, and treatment of patients with GAD, with emphasis on emerging insights that can benefit the primary care physician.

RECOGNITION OF GAD

An estimated 9 million Americans will suffer from GAD at some point during their lives.[1] This high rate of

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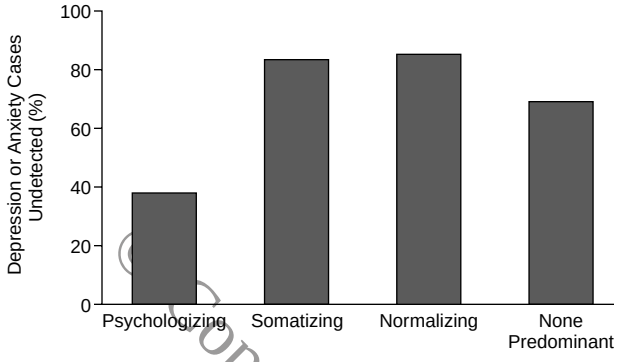
Figure 1. Symptom Attribution and Recognition of Anxiety and Depression by the Primary Care Physician[a]



[a]Based on data from Kessler et al.[12]

occurrence has been confirmed in studies of primary care patients. Use of the Primary Care Evaluation of Mental Disorders (PRIME-MD) found that 18% of visiting patients suffered from an anxiety disorder, including 7% with GAD,[2] and a World Health Organization (WHO)-sponsored international study found that selected anxiety disorders, including GAD, affected 10% of primary care patients.[3] Kessler and Wittchen[65] have reviewed primary care studies and conclude that GAD is the most frequent anxiety disorder presenting in primary care. Unfortunately, primary care physicians rarely recognize GAD.[65] In a study of 6370 primary care patients, Fifer et al.[4] found that 33% reported significant anxiety symptoms, but the symptoms were unrecognized and untreated in 56% of these patients and were associated with decreased functioning and well-being.

The reasons behind the underrecognition of GAD in primary care are numerous, as indicated by deGruy in a seminal report to the Institute of Medicine.[5] These reasons include the extent of physician knowledge, insurance regulations, time pressures, symptom attribution, perceptions of psychiatric disorders, the natural history of GAD, the diagnostic criteria applied, and frequent comorbidity.

Physician Knowledge

It is rare that a primary care physician knows or uses criteria from the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) in practice.[6] As a result, they may lack sufficient knowledge to recognize GAD accurately.

Insurance Regulations

Restrictive regulations, for example excluding payment for mental health care to primary care providers, may play a part in underrecognition of GAD or in the deliberate miscoding of mental diagnoses. A survey has reported that half (50.3%) of primary care clinicians had miscoded at least 1 visit in the previous 2 weeks.[7]

Time Pressures

The care of psychiatric problems often requires longer than the average primary care visit, which typically lasts 13 minutes during which several concerns may be presented.[5] With "competing demands" in this limited timeframe, the care of physical problems is often viewed as most pressing, and consideration of mental health concerns is deferred.[8–10] Thus, the realities of daily practice contribute substantially to the underrecognition of GAD.

Symptom Attribution

In 1985, Bridges and Goldberg[11] described the classic finding that, among patients with psychiatric diagnoses underlying their problems, 83% present with physical symptoms and 17% present with psychological complaints. Primary care physicians correctly recognize the psychiatric disorder in only 50% of patients with physical symptoms compared with 94% of those with psychological symptoms.

In 1999, Kessler et al.[12] extended this insight by classifying patient attributions by their presenting symptoms as either physical, psychological, or normalizing. An example of the latter would be a patient attributing difficulty sleeping to the normal consequence of work pressures. Figure 1 shows percentages for symptom attribution and recognition of anxiety and depression by the primary care physician. In contrast, of the 305 patients with anxiety or depression, 5% of patients attributed their complaints to somatic symptoms, 23% of patients to psychological symptoms, and 48% of patients used a normalizing attribution; 24% of patients used no predominant attributional style.[12] Furthermore, as the degree of normalizing increased, the likelihood that the physician recognized the underlying psychiatric disorder markedly decreased. Thus, primary care physicians unwittingly collude with their patients in the denial of psychiatric problems.

Perception of Psychiatric Illness

Patients and their families have strong biases that mitigate against recognition of mental health problems. The Surgeon General's recent landmark report on mental health found that a perceived stigma attached to the diagnosis of psychiatric disorders continued to be a major concern.[13]

Natural History of GAD

The course of GAD and the complex relationship between onset of the disorder, age, and sociodemographic factors[65] may contribute to the underrecognition or undertreatment of GAD.

Data from the HARP study, reported in this supplement[66] provide numerous insights into the presentation and natural history of anxiety disorders, including GAD. One insight of value to primary care physicians is that, while the average age of patients at onset of GAD is 21 years,[14] the age at presentation has a bimodal distribution. 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, it may be as late as 30 years.[15] Interestingly, Kessler and Wittchen[65] report that the age range of high risk for GAD extends into the mid-50s, which is older than for other anxiety disorders, and that over the past half century, GAD has become progressively more common.

In addition, the ability to recognize GAD may be further complicated by a link between the occurrence of GAD and social risk factors including unemployment, which is associated with taxing life circumstances such as family stress.[16] For patients with primary onset of GAD, often at a young age, the resulting psychiatric and secondary somatic distress is perceived as normal since they might never have experienced adult life untainted by anxiety. For the older patient, the explanatory power of adverse life circumstances often results in anxiety symptoms being considered as normal by both the patient and physician.[12] As the work of Keller[66] elegantly demonstrates, the natural history of GAD is chronic, with exacerbations often linked to increased life stresses. Although patients often visit their primary care physician for a variety of complaints, the underlying anxiety disorder is missed. The result for both the young and older patient with GAD is that they are deprived of the potential benefits of treatment.

Diagnostic Criteria and Comorbidity

Issues related to the diagnostic criteria for GAD, along with the high frequency of its comorbidity with depression, panic, and other anxiety disorders, influence not only the recognition of GAD, but also the resulting management decisions in primary care settings. The diagnostic criterion of required symptom duration for GAD has been the subject of controversy, as reviewed by Kessler and Wittchen.[65] These authors note that a 1-month requirement is best when identifying patients with significantly impaired function and that the current 6-month requirement in DSM-IV leads to the persistent exclusion of individuals whose symptoms wax and wane for long periods of time. These individuals might have both significant psychological suffering and functional impairment, but are never continuous at criterion levels for 6 months. The impact of this controversy is likely to be particularly important in primary care settings. Not only do primary care physicians often see patients early in the course of symptoms (frequently before 6 months have elapsed), but they are also potentially more likely to see those patients who have a waxing and waning course. Delayed recognition and treatment of GAD might contribute to the development of comorbidities and unhealthy self-medication practices.

Primary care physicians often fail to recognize GAD even when they properly diagnose the more striking symptoms of depression or panic attacks, which are frequently comorbid with GAD.[14–17,66] As Kessler and Wittchen[65] note, the underlying worry of GAD might lead patients to discuss their symptoms of depression, panic, or other anxiety disorders with their primary care physicians while not recognizing that the worry itself should be a focus of discussion. Although a number of core symptoms are common to GAD, major depression, and other anxiety disorders, Kessler and Wittchen[65] and others[18] have clearly demonstrated that GAD is a separate and distinct clinical disorder, including as it presents in primary care settings.[19]

Comorbidity dramatically affects patients. For example, one study indicated greater impairment and persistence of major depression when comorbid with GAD.[20] At 1-year follow-up, depressed patients with coexisting anxiety had experienced 54.9 disability days and 82% continued to be depressed, compared with 19.8 disability days and persistence of depression in 57% of those without comorbid anxiety. Keller and Hanks[21] have reported that, compared with a 13-week mean time to recovery among depressed nonanxious patients, those with coexisting depression and high anxiety had a mean episode duration of 26 weeks.

The recognition of GAD in comorbid patients therefore has important management implications. While there is overlap in the therapeutic efficacy of some agents used for treating depression and other anxiety disorders, the lack of recognition of the underlying GAD can lead physicians to choose suboptimal therapies or to exclude appropriate therapeutic goals related to GAD in their management of patients. Furthermore, patients will not be educated regarding the expected chronic course of GAD or given a satisfactory explanation of the symptoms they experience. Recognition of comorbidity, and the likelihood that it leads to greater impairment and greater persistence of psychiatric disorders, should influence decisions on treatment strategy, including the duration of initial treatment and the potential requirement for long-term maintenance therapy in comorbid patients. Thus, while the highly comorbid nature of GAD contributes to its underrecognition, it also increases the importance of its accurate diagnosis.

MANAGEMENT

In addition to definitive pharmacologic or psychological treatment, the proper management of GAD in the primary care setting includes education of patients and their families, counseling regarding associated problems, and ongoing support. In addition, patients suffering from GAD are likely to need help in managing insomnia and developing coping strategies to manage their worries.

Education and Counseling

Education and counseling are critical to helping patients achieve control of their anxiety and adhere to treatment. Basic education about the nature of anxiety disorders using an illness model that is understandable to patients can be helpful. Enabling patients and their families to appreciate GAD as a medical condition amenable to therapeutic

Table 1. Stimulus Control Therapy Steps for Combating Insomnia[a]

Step 1	Lie down, intending to go to sleep, only when you are sleepy.
Step 2	Do not use your bed for anything but sleep with the exception of sexual activity or, if allowed, reading.[b]
Step 3	If unable to fall asleep easily, get up and go to another room. Stay up as long as needed and return to the bedroom only when you feel ready to fall asleep.

[a]Based on data from Bootzin et al.[33]
[b]If reading is allowed, the reading material should be interesting but not stimulating. Reading as long as possible, fighting sleep, is often best. This promotes the association between reading, turning the lights off, and rapidly falling asleep.

intervention is particularly useful in allaying stigmatizing concerns or fears that it reflects moral weakness or other character flaws.[13] Moreover, information about the chronic but waxing and waning nature of the disorder might help patients reflect on their personal histories, make it easier for them to accept long-term treatment, and sensitize patients who respond well to treatment to an awareness of early signs of relapse or recurrence. As appropriate, education about GAD should be integrated with helping the individual understand any comorbid disorders.

Counseling to encourage several modifications in lifestyle can be beneficial to patients with GAD. Inquiry regarding the use of alcohol or other sedating agents and about stimulants, including nicotine, coffee, and other caffeinated beverages, can lead to brief counseling about moderating use or the need for more aggressive intervention. The anxious patient might benefit significantly from adopting a regular exercise program. In a meta-analysis of the effects of exercise on anxiety in depressed patients, regular exercise proved as effective as pharmacologic treatment.[22] While similar data are not available specifically for patients with GAD, clinical experience supports the recommendation of exercise to reduce stress and anxiety, as well as to improve sleep.

Managing Insomnia

Insomnia, either acute or chronic, is the norm among patients with GAD. While most individuals fall asleep within 20 to 30 minutes, the patient with GAD will report sleep latency of 1 hour or more.[23] The physician should inquire into destructive self-treatment, including use of alcohol and medications, and brief assessment of insomnia should include determining the pattern of sleep difficulty.[23] For example, the anxious depressed patient may have difficulty with both going to sleep and early awakening, and those with comorbid posttraumatic stress disorder often fear going to sleep because of nightmares.[24] Frequent awakening may indicate a medical condition that, for example, causes pain, respiratory distress, or the need for frequent urination.[25] Patients with anxiety also might not recognize contributory factors such as environmental noise, light, or uncomfortable temperature. In addition, nicotine serves as a stimulant, and its withdrawal is a physiologic stressor—accounting for the heavy smoker who has difficulty going to sleep after his or her bedtime smoke or after smoking during an awakening in the night. Asking patients about daytime sleepiness and problems in functioning due to tiredness can help the physician understand and monitor the severity of insomnia.

Insomnia may be a consequence of both GAD and patients' frequently comorbid depression.[26] Acute stressors such as marital or work difficulties can precipitate acute insomnia in anxious individuals. Their propensity to worry can then lead to chronic insomnia and maladaptive habits such as poor "sleep hygiene" or use of alcohol, which lead to persistence of insomnia even after the acute stressors resolve. Furthermore, insomnia has been linked in several studies to the development or recurrence of depression.[27–30] Identifying insomnia and helping patients with GAD who experience sleep disturbance are therefore important components of their care.

In treating the insomnia of patients with GAD, the physician's priority should be to help individuals develop lifestyle changes that will promote its long-term control. Sleep restriction and stimulus control are 2 approaches that have proved to be most helpful, providing benefit similar to hypnotic medications but more enduring.[31,32] Sleep restriction requires patients to limit their total time in bed to that required before the development of insomnia. This has been shown to result in deeper sleep, fewer awakenings, and greater daytime alertness. A number of stimulus control approaches have been proposed, and an outline of one method demonstrated to be effective is shown in Table 1.[33] As discussed above, another helpful approach is regular exercise, ideally performed 5 to 6 hours before bedtime. Improvement is progressive, often with marked effect after 4 to 6 weeks of regular exercise. Patients fall asleep more easily, awake less, shift their sleep content from light to more restful deep (stage 3 and 4) sleep, and feel more rested during the day.[34,35] Finally, the simple instruction to put the alarm clock where it cannot be seen when lying in bed can help patients avoid focusing on the time and worrying about the insomnia.

At the time of initial diagnosis (particularly if difficulty sleeping was a presenting complaint) or at times of acute exacerbation of insomnia or anxiety symptoms, patients often require short-term pharmacologic therapy for their insomnia. This can be beneficial in helping individuals adhere to other treatment recommendations for GAD and comorbid disorders. Indeed, at times, patients will accept treatment for insomnia before they will accept treatment for the underlying psychiatric disorder(s). In situations requiring short-term pharmacologic treatment of insomnia, use of one of the nonbenzodiazepine benzodiazepine receptor agonists, zolpidem or zaleplon, is often beneficial.[26] Of these, zaleplon is the most rapidly eliminated,

Table 2. Managing Worry to Improve Coping

Set aside ½ hour to organize worries
Jot down worries on 3 × 5 cards as they come to mind
Organize worries into:
Minor worries and hassles (eg, returning calls, making appointments, paying bills)
Schedule in next few days
Larger worries (eg, financial, family, occupational)
Identify priorities
Identify first or next steps

allowing it to be taken as needed, even in the middle of the night. Memory performance and reaction time 4 hours after such middle-of-the-night dosing are no different from placebo, nor is driving impaired.[36,37] For patients with persistent insomnia, further assessment by and referral to a sleep specialist are appropriate.

Development of Coping Strategies

Patients with GAD often find themselves rehashing problems and unmet expectations. During exacerbations, such worry can become overwhelming and their normal coping ability and purposeful planning capacity may be immobilized. A simple routine such as that presented in Table 2 can help patients organize, prioritize, and plan simple next steps to address their challenges. Practiced regularly, it provides a familiar approach that can help patients in times of crisis and can lead to an improved sense of coping and self-control.

These simple educational and counseling strategies can help primary care physicians develop the ability of patients with GAD to self-manage. However, while they are approaches that patients often find beneficial, they do not replace the need for proven effective therapy. Indeed, without such therapy patients might not be able to productively use these supportive approaches.

TREATMENT

Individuals suffering from GAD deserve effective treatment.[38] As primary care physicians initiate such treatment, they should clarify the goals.[39] Short term, these should include a reduction of somatic symptoms, relief from psychic distress such as overwhelming worry, and resolution of symptoms such as insomnia. An additional goal is to minimize treatment adverse events, both in the short term (e.g., worsening insomnia, agitation) and long term (e.g., weight gain, sexual dysfunction). Long-term goals should include attaining full functional status unencumbered by anxiety.[40–42] For the patient with an onset of GAD during adolescence, this might include exploring new adult roles for the first time. Additional long-term goals are the prevention of relapse or recurrence and relief from the comorbid disorders, such as depression or panic disorder, from which most patients suffer.

Approaches to the treatment of GAD have been reviewed by Gorman.[67] There is strong evidence for the effectiveness of pharmacotherapy, cognitive-behavioral therapy (CBT), and relaxation techniques, providing validation that the long-term goal of full recovery is attainable by many patients with GAD.[13] However, unfortunately, as Keller[66] discusses, few patients currently receive such therapeutic benefits. Thus, an important role that the primary care physician is well situated to fulfill is to follow patients with GAD over the long term, assisting them in taking advantage of treatment and pursuing treatment to recovery.

Cognitive-Behavioral Therapy

While formal CBT has been demonstrated to provide benefit,[43–46] few primary care patients with GAD receive CBT as a consequence of reimbursement policies, time, and other constraints. Although it is unrealistic for the primary care physician to provide CBT, an awareness of its principles can be useful in counseling patients with GAD, particularly those who are high utilizers of health care resources or suffering from acute exacerbations. These principles include helping patients to identify and correct their misconceptions about events they perceive as worrying, and the automatic thought processes that underlie the misconceptions, and to develop self-regulation of these thoughts, feelings, and behaviors. For example, a patient might perceive a change in duties in a job or home situation, which in reality is minor, as likely to develop into a major catastrophe. Discussing the basis of the patient's misinterpretation and their sense of loss of control might be helpful.

For patients who choose CBT, the primary care physician has several roles. The first is helping patients to select experienced therapists with expertise in utilizing CBT for GAD. For many patients, combining CBT with pharmacotherapy early on in therapy is a desired strategy, particularly for those with severe symptoms. In such cases, primary care physicians might prescribe and monitor pharmacotherapy in coordination with patients' therapists. A long-term role for primary care physicians is to help patients continue to use the therapeutic approaches learned in CBT following the conclusion of formal therapy, particularly as they encounter new stressors.

Pharmacotherapy

For most patients, pharmacotherapy is the treatment chosen. As discussed above, attaining both short- and long-term effectiveness and minimizing adverse effects should guide selection of appropriate agents. The serotonin-norepinephrine reuptake inhibitor (venlafaxine), selective serotonin reuptake inhibitors (SSRIs), buspirone, and benzodiazepines are agents commonly used in primary care. Tricyclic antidepressants and monoamine oxidase inhibitors, because of their potential for lethal overdosage and serious adverse events, should be reserved for patients not responding to other agents.

Although benzodiazepines provide rapid onset of action, their use by patients with GAD has several drawbacks.[47] While their sedating properties provide immediate relief from insomnia and the somatic symptoms resulting from tension and stress, they have less effect on psychic symptoms, including worry.[48–50] It is therefore not surprising that patients often report a rapid relapse of symptoms following the discontinuation of benzodiazepines.[51] Consequently, patients seek to continue them long term, with resulting problems of habituation and withdrawal and often associated conflict with their primary care providers. Long-term use can also result in other significant adverse effects, including persistent cognitive impairment, increased likelihood of falling, and decreased driving performance.[52] Moreover, patients with GAD are highly likely to have, or be at risk of developing, comorbid depression, for which benzodiazepines are ineffective as a treatment (and indeed may increase the risk of developing depression), which further weighs against their use for GAD.

Buspirone, while effective in treating GAD, has a delayed onset of action of several weeks and does not treat other comorbid anxiety or depressive disorders. Consequently, its use seems limited to the unusual primary care patient who suffers from isolated GAD and, due to the short half-life of buspirone, does not mind taking medication several times a day. Of the SSRIs, paroxetine is the most studied agent and the one that has been indicated for the short-term treatment of GAD. Paroxetine treats other anxiety disorders and depression, so it can be a useful agent for the primary care patient with GAD and comorbidities.[53,54] However, the primary care physician prescribing paroxetine should alert the patient to its potential to cause long-term weight gain. In several studies, 20% to 25% of patients treated with paroxetine for 6 months experienced weight gain of > 7% of their initial weight (approximately 10 lb [4.5 kg] for an average 140-lb [63.5-kg] person).[55,56] In addition, paroxetine is the most likely of the SSRIs to result in withdrawal symptoms should the patient omit a dose.[57] While other SSRIs devoid of the associated difficulties of weight gain and withdrawal might be effective in GAD, we do not currently have data demonstrating their efficacy.

Venlafaxine (75–225 mg/day) has been indicated for the long-term treatment of GAD, and both short- and long-term efficacy in treating GAD has been demonstrated.[47,58] An impressive finding in studies is the progression of patients from response (>50% reduction in symptoms) to remission (Hamilton Rating Scale for Anxiety ≤ 7).[59,60] Venlafaxine has also been demonstrated to be effective in treating depression and depressive symptoms in patients with GAD.[61] Consequently, it is a valuable first-line treatment option for primary care physicians. Those prescribing venlafaxine should titrate the dosage to minimize potential adverse events (nausea, dizziness, dry mouth, sleepiness) and should monitor patients for a significant increase in blood pressure, particularly at doses above 150 mg/day.[62] Fortunately, blood pressure increases are unusual (occurring in < 3% of patients) and appear to be dose related.

In treating patients with GAD and comorbidities, the primary care physician should emphasize the need for extended treatment. Patients are likely to report a major decrease in impairment over the first 2 to 3 months and often discontinue their medication because they feel it is no longer needed. However, early discontinuation is highly likely to lead to relapse. For instance, 50% of depressed patients who responded and then discontinued their medication at 6 weeks will relapse within 1 year, compared with only about 10% to 15% who continued treatment.[63] As Keller[66] has noted, remission does not necessarily lead to immediate improvement in functioning. Much longer-term treatment is often required to support patients in learning or resuming normal functional roles. Primary care physicians should encourage the continuation of treatment and monitor patients' progress in attaining not only remission from all symptoms but also full functional recovery.[42]

CONCLUSION

A total of 39% of patients suffering from GAD are markedly impaired as measured by the Social Disability Schedule (which includes measures such as energy and performance, contact with coworkers, and daily activities),[19] and, as Kessler and others report, patients with GAD are often high utilizers of health care resources.[64,65] In primary care settings, the majority of patients with GAD will also suffer from depression or other anxiety disorders and experience a very chronic waxing and waning course. The chronicity of GAD often contributes to its lack of recognition as a treatable disorder, both by the patient and the primary care physician. Agents such as venlafaxine, which has been demonstrated to be effective in leading to remission and improving function, provide primary care physicians with an effective treatment option that can markedly improve the quality of life for patients with GAD.

Drug names: paroxetine (Paxil), venlafaxine (Effexor), zaleplon (Sonata), zolpidem (Ambien).

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