

# Anxiety Disorders: Understanding Your Path to Calm

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June 17, 2026

## RECOMMENDED CITATION

mohammad looti (2026). *Anxiety Disorders: Understanding Your Path to Calm*.  
PSYCHOLOGICAL SCALES. Retrieved from <https://scales.arabpsychology.com/?p=38605>

Anxiety disorders are blanket terms covering several different forms of abnormal and pathological fear and anxiety which only came under the aegis of psychiatry at the very end of the 19th century. Gelder, Mayou & Geddes (2005) explains that anxiety disorders are classified in two groups: continuous symptoms and episodic symptoms. Current psychiatric diagnostic criteria recognize a wide variety of anxiety disorders. Recent surveys have found that as many as 18% of Americans may be affected by one or more of them.

The term anxiety covers four aspects of experiences an individual may have: mental apprehension, physical tension, physical symptoms and dissociative anxiety (symptoms associated with hyperventilation). Anxiety disorder is divided into generalized anxiety, phobic, and panic disorders; each has its own characteristics and symptoms and they require different treatment (Gelder et al. 2005). The emotions present in anxiety disorders range from simple nervousness to bouts of terror (Barker 2003).

Standardized screening clinical questionnaires such as Zung Self-Rating Anxiety Scale can be used to detect anxiety symptoms, and suggest the need for a formal diagnostic assessment of anxiety disorder.

## **Classification**

### **Generalized anxiety disorder**

Generalized anxiety disorder (GAD) is a common chronic disorder characterized by long-lasting anxiety that is not focused on any one object or situation. Those suffering from generalized anxiety experience non-specific persistent fear and worry and become overly concerned with everyday matters. Generalized anxiety disorder is the most common anxiety disorder to affect older adults. Anxiety can be a symptom of a medical or substance abuse problem, and medical professionals must be aware of this. A diagnosis of GAD is made when a person has been excessively worried about an everyday problem for six months or more. A person may find they have problems making daily decisions and remembering commitments as a result of lack of concentration/preoccupation with worry. Appearance looks strained, skin is pale with increased sweating from the hands, feet and axillae. May be tearful which can suggest depression. Before a diagnosis of anxiety disorder is made, nurses and physicians must rule out drug-induced anxiety and medical causes.

### **Panic disorder**

In panic disorder, a person suffers from brief attacks of intense terror and apprehension, often marked by trembling, shaking, confusion, dizziness, nausea, difficulty breathing. These panic attacks, defined by the APA as fear or discomfort that abruptly arises and peaks in less than ten minutes, can last for several hours and can be triggered by stress, fear, or even exercise; the specific cause is not always apparent.

In addition to recurrent unexpected panic attacks, a diagnosis of panic disorder requires that said attacks have chronic consequences: either worry over the attacks' potential implications, persistent fear of future attacks, or significant changes in behavior related to the attacks. Accordingly, those suffering from panic disorder experience symptoms even outside specific panic episodes. Often, normal changes in heartbeat are noticed by a panic sufferer, leading them to think something is wrong with their heart or they are about to have another panic attack. In some cases, a heightened awareness (hypervigilance) of body functioning occurs during panic attacks, wherein any perceived physiological change is interpreted as a possible life-threatening illness (i.e., extreme hypochondriasis). However, with the correct professional help 70%-90% of those suffering from panic disorder are helped in 6-8 weeks.

### **Panic disorder with agoraphobia**

A person experiences an unexpected panic attack, then has substantial anxiety over the possibility of having another attack. The person fears and avoids whatever situation might induce a panic attack. The person may never or rarely leave their home to prevent a panic attack they believe to be inescapable, extreme terror.

### **Phobias**

The single largest category of anxiety disorders is that of phobic disorders, which includes all cases in which fear and anxiety is triggered by a specific stimulus or situation. Between 5% and 12% of the population worldwide suffer from phobic disorders. Sufferers typically anticipate terrifying consequences from encountering the object of their fear, which can be anything from an animal to a location to a bodily fluid to a particular situation. Sufferers understand that their fear is not proportional to the actual potential danger but still are overwhelmed by the fear.

### **Agoraphobia**

Agoraphobia is the specific anxiety about being in a place or situation where escape is difficult or embarrassing or where help may be unavailable. Agoraphobia is strongly linked with panic disorder and is often precipitated by the fear of having a panic attack. A common manifestation involves needing to be in constant view of a door or other escape route. In addition to the fears themselves, the term agoraphobia is often used to refer to avoidance behaviors that sufferers often develop. For example, following a panic attack while driving, someone suffering from agoraphobia may develop anxiety over driving and will therefore avoid driving. These avoidance behaviors can often have serious consequences; in severe cases, one can be confined to one's home.

### **Social anxiety disorder**

Social anxiety disorder (SAD; also known as social phobia) describes an intense fear and avoidance of negative public scrutiny, public embarrassment, humiliation, or social interaction. This fear can be specific to particular social situations (such as public speaking) or, more typically, is experienced in most (or all) social interactions. Social anxiety often manifests specific physical symptoms, including blushing, sweating, and difficulty speaking. Like with all phobic disorders, those suffering from social anxiety often will attempt to avoid the source of their anxiety; in the case of social anxiety this is particularly problematic, and in severe cases can lead to complete social isolation.

### **Obsessive-compulsive disorder**

Obsessive-compulsive disorder (OCD) is a type of anxiety disorder primarily characterized by repetitive obsessions (distressing, persistent, and intrusive thoughts or images) and compulsions (urges to perform specific acts or rituals). It affects roughly around 3% of the population worldwide. The OCD thought pattern may be likened to superstitions insofar as it involves a belief in a causative relationship where, in reality, one does not exist. Often the process is entirely illogical; for example, the compulsion of walking in a certain pattern may be employed to alleviate the obsession of impending harm. And in many cases, the compulsion is entirely inexplicable, simply an urge to complete a ritual triggered by nervousness.

In a slight minority of cases, sufferers of OCD may only experience obsessions, with no overt compulsions; a much smaller number of sufferers experience only compulsions.

### **Post-traumatic stress disorder**

Post-traumatic stress disorder (PTSD) is an anxiety disorder which results from a traumatic experience. Post-traumatic stress can result from an extreme situation, such as combat, natural disaster, rape, hostage situations, more serious kinds of child abuse, or even a serious accident. It can also result from long term (chronic) exposure to a severe stressor, for example soldiers who endure individual battles but cannot cope with continuous combat. Common symptoms include hypervigilance, flashbacks, avoidant behaviors, anxiety, anger and depression. There are a number of treatments which form the basis of the care plan for those suffering with PTSD. Such treatments include cognitive behavioral therapy (CBT), psychotherapy and support from family and friends. These are all examples of treatments used to help people suffering from PTSD.

### **Separation anxiety**

Separation anxiety disorder (SepAD) is the feeling of excessive and inappropriate levels of anxiety over being separated from a person or place. Separation anxiety is a normal part of development

in babies or children, and it is only when this feeling is excessive or inappropriate that it can be considered a disorder. Separation anxiety disorder affects roughly 7% of adults and 4% of children, but the childhood cases tend to be more severe, in some instances even a brief separation can produce panic.

### **Childhood anxiety disorders**

Children as well as adults experience feelings of anxiousness, worry and fear when facing different situations, especially those involving a new experience. However, if anxiety is no longer temporary and begins to interfere with the child's normal functioning or do harm to their learning, the problem may be more than just an ordinary anxiousness and fear common to the age.

When children suffer from a severe anxiety disorder their thinking, decision-making ability, perceptions of the environment, learning and concentration get affected. They not only experience fear, nervousness, and shyness but also start avoiding places and activities. Anxiety also raises blood pressure and heart rate and can cause nausea, vomiting, stomach pain, ulcers, diarrhea, tingling, weakness, and shortness of breath. Some other symptoms are frequent self-doubt and self-criticism, irritability, sleep problems and, in extreme cases, thoughts of not wanting to be alive.

If these children are left untreated, they face risks such as poor results at school, avoidance of important social activities, and substance abuse. Children who suffer from an anxiety disorder are likely to suffer other disorders such as depression, eating disorders, and attention deficit disorders, both hyperactive and inattentive.

About 13 of every 100 children and adolescents between 9 to 17 years experience some kind of anxiety disorder, and girls are more affected than boys. The basic temperament of children may be key in some of their childhood and adolescent disorders.

Research in this area is very difficult to perform because as children grow their fears change, making it difficult for researchers to obtain enough data and thus more reliable results. For instance, between the ages of 6 and 8, children's fear of the dark and imaginary creatures decreases, but they become more anxious about school performance and social relationships. If children experience an excessive amount of anxiety during this stage, this could lead to development of anxiety disorders later in life.

According to research, childhood anxiety disorders are caused by biological and psychological factors. Also, it is suggested that when children have a parent with anxiety disorders, they are more likely to have an anxiety disorder, too. Stress can trigger anxiety disorders, and children and adolescents with anxiety disorders seem to have an increased physical and psychological reaction to stress. Their reaction to danger, even if it is a small one, is quicker and stronger.

## Causes

### Biological

Low levels of GABA, a neurotransmitter that reduces activity in the central nervous system, contribute to anxiety. A number of anxiolytics achieve their effect by modulating the GABA receptors.

Selective serotonin reuptake inhibitors, the drugs most commonly used to treat depression, are frequently considered as a first line treatment for anxiety disorders. A 2004 study using functional brain imaging techniques suggests that the effects of SSRIs in alleviating anxiety may result from a direct action on GABA neurons rather than as a secondary consequence of mood improvement.

Severe anxiety and depression can be induced by sustained alcohol abuse which in most cases abates with prolonged abstinence. Even moderate, sustained alcohol use may increase anxiety and depression levels in some individuals. Caffeine, alcohol and benzodiazepine dependence can worsen or cause anxiety and panic attacks. In one study in 1988-1990, illness in approximately half of patients attending mental health services at one British hospital psychiatric clinic, for conditions including anxiety disorders such as panic disorder or social phobia, was determined to be the result of alcohol or benzodiazepine dependence. In these patients, an initial increase in anxiety occurred during the withdrawal period followed by a cessation of their anxiety symptoms.

Intoxication from stimulants is likely to be associated with repetitive panic attacks.

There is evidence that chronic exposure to organic solvents in the work environment can be associated with anxiety disorders. Painting, varnishing and carpet-laying are some of the jobs in which significant exposure to organic solvents may occur.

People with obsessive-compulsive disorder (sometimes considered an anxiety disorder), evince increased grey matter volumes in bilateral lenticular nuclei, extending to the caudate nuclei, while decreased grey matter volumes in bilateral dorsal medial frontal/anterior cingulate gyri. These findings contrast with those in people with other anxiety disorders, who evince decreased (rather than increased) grey matter volumes in bilateral lenticular/caudate nuclei, while also decreased grey matter volumes in bilateral dorsal medial frontal/anterior cingulate gyri.

### Amygdala

The amygdala is central to the processing of fear and anxiety, and its function may be disrupted in anxiety disorders. Sensory information enters the amygdala through the nuclei of the basolateral complex (consisting of lateral, basal, and accessory basal nuclei). The basolateral complex processes sensory-related fear memories and communicates their threat importance to memory

and sensory processing elsewhere in the brain, such as the medial prefrontal cortex and sensory cortices.

Another important area is the adjacent central nucleus of the amygdala, which controls species-specific fear responses, via connections to the brainstem, hypothalamus, and cerebellum areas. In those with general anxiety disorder, these connections functionally seem to be less distinct, with greater gray matter in the central nucleus. Another difference is that the amygdala areas have decreased connectivity with the insula and cingulate areas that control general stimulus salience, while having greater connectivity with the parietal cortex and prefrontal cortex circuits that underlie executive functions.

The latter suggests a compensation strategy for dysfunctional amygdala processing of anxiety. Researchers have noted "Amygdalofrontoparietal coupling in generalized anxiety disorder patients may ... reflect the habitual engagement of a cognitive control system to regulate excessive anxiety." This is consistent with cognitive theories that suggest the use in this disorder of attempts to reduce the involvement of emotions with compensatory cognitive strategies.

Clinical and animal studies suggest a correlation between anxiety disorders and difficulty in maintaining balance. A possible mechanism is malfunction in the parabrachial nucleus, a brain structure that, among other functions, coordinates signals from the amygdala with input concerning balance.

Anxiety processing in the basolateral amygdala has been implicated with dendritic arborization of the amygdaloid neurons. SK2 potassium channels mediate inhibitory influence on action potentials and reduce arborization. By overexpressing SK2 in the basolateral amygdala, anxiety in experimental animals can be reduced together with general levels of stress-induced corticosterone secretion.

## **Stress**

Anxiety disorder can arise in response to life stresses such as financial worries or chronic physical illness. Somewhere between 4% and 10% of older adults are diagnosed with anxiety disorder, a figure that is probably an underestimate due to the tendency of adults to minimize psychiatric problems or to focus on their physical manifestations. Anxiety is also common among older people who have dementia. On the other hand, anxiety disorder is sometimes misdiagnosed among older adults when doctors misinterpret symptoms of a physical ailment (for instance, racing heartbeat due to cardiac arrhythmia) as signs of anxiety.

## **Diagnosis**

Anxiety disorders are often debilitating chronic conditions, which can be present from an early age or begin suddenly after a triggering event. They are prone to flare up at times of high stress and are frequently accompanied by physiological symptoms such as headache, sweating, muscle spasms, palpitations, and hypertension, which in some cases lead to fatigue or even exhaustion.

In casual discourse the words "anxiety" and "fear" are often used interchangeably; in clinical usage, they have distinct meanings: "anxiety" is defined as an unpleasant emotional state for which the cause is either not readily identified or perceived to be uncontrollable or unavoidable, whereas "fear" is an emotional and physiological response to a recognized external threat. The term "anxiety disorder" includes fears (phobias) as well as anxieties.

Anxiety disorders are often comorbid with other mental disorders, particularly clinical depression, which may occur in as many as 60% of people with anxiety disorders. The fact that there is considerable overlap between symptoms of anxiety and depression, and that the same environmental triggers can provoke symptoms in either condition, may help to explain this high rate of comorbidity.

Studies have also indicated that anxiety disorders are more likely among those with family history of anxiety disorders, especially certain types.

Sexual dysfunction often accompanies anxiety disorders, although it is difficult to determine whether anxiety causes the sexual dysfunction or whether they arise from a common cause. The most common manifestations in individuals with anxiety disorder are avoidance of intercourse, premature ejaculation or erectile dysfunction among men and pain during intercourse among women. Sexual dysfunction is particularly common among people affected by panic disorder (who may fear that a panic attack will occur during sexual arousal) and posttraumatic stress disorder.

## **Treatment**

The most important clinical point to emerge from studies of social anxiety disorder is the benefit of early diagnosis and treatment. Social anxiety disorder remains under-recognized in primary care practice, with patients often presenting for treatment only after the onset of complications such as clinical depression or substance abuse disorders.

Treatment options available include lifestyle changes; psychotherapy, especially cognitive behavioral therapy; and pharmaceutical therapy. Education, reassurance and some form of cognitive-behavioral therapy should almost always be used in treatment. Research has provided evidence for the efficacy of two forms of treatment available for social phobia: certain medications and a specific form of short-term psychotherapy called cognitive-behavioral therapy (CBT), the central component being gradual exposure therapy.

## Psychotherapy

Research has shown that cognitive-behavioral therapy (CBT) can be highly effective for several anxiety disorders, particularly panic disorder and social phobia. CBT, as its name suggests, has two main components: cognitive and behavioral. In cases of social anxiety, the cognitive component can help the patient question how they can be so sure that others are continually watching and harshly judging him or her. The behavioral component seeks to change people's reactions to anxiety-provoking situations.

As such it serves as a logical extension of cognitive therapy, whereby people are shown proof in the real world that their dysfunctional thought processes are unrealistic. A key element of this component is gradual exposure, in which the patient is confronted by the things they fear in a structured, sensitive manner. Gradual exposure is an inherently unpleasant technique; ideally it involves exposure to a feared social situation that is anxiety provoking but bearable, for as long as possible, two to three times a week. Often, a hierarchy of feared steps is constructed and the patient is exposed to each step sequentially.

The aim is to learn from acting differently and observing reactions. This is intended to be done with support and guidance, and when the therapist and patient feel they are ready. Cognitive-behavioral therapy for social phobia also includes anxiety management training, which may include techniques such as deep breathing and muscle relaxation exercises, which may be practiced 'in-situ'. CBT can also be conducted partly in group sessions, facilitating the sharing of experiences, a sense of acceptance by others and undertaking behavioral challenges in a trusted environment (Heimberg).

Some studies have suggested social skills training can help with social anxiety. However, it is not clear whether specific social skills techniques and training are required, rather than just support with general social functioning and exposure to social situations.

Additionally, a recent study has suggested that interpersonal therapy, a form of psychotherapy primarily used to treat depression, may also be effective in the treatment of social phobia.

Extensive research supports the neural plasticity of the brain in reaction to stressful experiences. A treatment and prevention method called Adaptive Behavioral therapy is based on understanding the adaptations which occur in developmental years due to stressful experiences and the brain's ability to create new reactions to the same stressor. In this treatment a time gap between when information is received by the brain (stress trigger) and the decision for behavior is widened to allow a re-evaluation to occur as a stressful experience is taking place. This new time to reprocess information is referred to as a Pivotal Moment when new behavior can be consciously created. The development of new adaptive behavior is promoted through the use of interruption techniques and specific tools.

Treatment is structured around a self report notebook which is used to collect historic and current stress patterns of response. Treatment is guided by the therapist in a direct manner in sessions and experiences between sessions are used to provide new experimental behavior. Adaptive behavioral therapy is also used as a preventive treatment. Practice with smaller stressors creates familiarity with healthy adaptive responses for future use.

## Medications

When medication is indicated, SSRIs are generally recommended as first line agents. SNRIs such as venlafaxine (Effexor) are also effective. Benzodiazepines are also sometimes indicated for short-term or PRN use. They are usually considered as a second-line treatment due to disadvantages such as cognitive impairment and due to their risks of dependence and withdrawal problems. MAOIs such as phenelzine (Nardil) and tranylcypromine (Parnate) are considered an effective treatment and are especially useful in treatment-resistant cases, however, dietary restrictions and medical interactions may limit their use. There is evidence that certain newer medications including the GABA analogue pregabalin (Lyrica) and the novel antidepressant mirtazapine (Remeron) are effective treatments for anxiety disorders. TCAs such as imipramine, as well as atypical antipsychotics such as quetiapine, and piperazines such as hydroxyzine are occasionally prescribed.

These medications need to be used with extreme care among older adults, who are more likely to suffer side effects because of coexisting physical disorders. Adherence problems are more likely among elderly patients, who may have difficulty understanding, seeing, or remembering instructions.

## SSRIs

Selective serotonin reuptake inhibitors (SSRIs), a class of antidepressants, are considered by many to be the first choice medication for generalised social phobia. These drugs elevate the level of the neurotransmitter serotonin, among other effects. The first drug formally approved by the Food and Drug Administration was paroxetine, sold as Paxil in the U.S. or Seroxat in the UK. Compared to older forms of medication, there is less risk of tolerability and drug dependency. However, their efficacy and increased suicide risk has been subject to controversy.

In a 1995 double-blind, placebo-controlled trial, the SSRI paroxetine was shown to result in clinically meaningful improvement in 55% of patients with generalized social anxiety disorder, compared with 23.9% of those taking placebo. An October 2004 study yielded similar results. Patients were treated with either fluoxetine, psychotherapy, fluoxetine and psychotherapy, placebo and psychotherapy, or a placebo. The first four sets saw improvement in 50.8% to 54.2% of the patients. Of those assigned to receive only a placebo, 31.7% achieved a rating of 1 or 2 on the

Clinical Global Impression-Improvement scale. Those who sought both therapy and medication did not see a boost in improvement.

General side-effects are common during the first weeks while the body adjusts to the drug. Symptoms may include headaches, nausea, insomnia and changes in sexual behavior. Treatment safety during pregnancy has not been established. In late 2004 much media attention was given to a proposed link between SSRI use and juvenile suicide. For this reason, the use of SSRIs in pediatric cases of depression is now recognized by the Food and Drug Administration as warranting a cautionary statement to the parents of children who may be prescribed SSRIs by a family doctor. Recent studies have shown no increase in rates of suicide. These tests, however, represent those diagnosed with depression, not necessarily with social anxiety disorder. However, due to the nature of the conditions, those taking SSRIs for social phobias are far less likely to have suicidal ideation than those with depression.

### **Other drugs**

Although SSRIs are often the first choice for treatment, other prescription drugs are used, sometimes only if SSRIs fail to produce any clinically significant improvement.

In 1985, before the introduction of SSRIs, anti-depressants such as monoamine oxidase inhibitors (MAOIs) were frequently used in the treatment of social anxiety. Their efficacy appears to be comparable or sometimes superior to SSRIs or benzodiazepines. However, because of the dietary restrictions required, high toxicity in overdose, and incompatibilities with other drugs, its usefulness as a treatment for social phobias is now limited. Some argue for their continued use, however, or that a special diet does not need to be strictly adhered to. A newer type of this medication, Reversible inhibitors of monoamine oxidase subtype A (RIMAs) inhibit the MAO enzyme only temporarily, improving the adverse-effect profile but possibly reducing their efficacy.

Benzodiazepines such as alprazolam and clonazepam are an alternative to SSRIs. These drugs are often used for short-term relief of severe, disabling anxiety. Although benzodiazepines are still sometimes prescribed for long-term everyday use in some countries, there is much concern over the development of drug tolerance, dependency and recreational abuse. It has been recommended that benzodiazepines are only considered for individuals who fail to respond to safer medications. Benzodiazepines augment the action of GABA, the major inhibitory neurotransmitter in the brain; effects usually begin to appear within minutes or hours.

The novel antidepressant mirtazapine has been proven effective in treatment of social anxiety disorder. This is especially significant due to mirtazapine's fast onset and lack of many unpleasant side-effects associated with SSRIs (particularly, sexual dysfunction).

In Japan, the serotonin-norepinephrine reuptake inhibitor (SNRI) Milnacipran is used in the

treatment of Taijin kyofusho a Japanese variant of social anxiety disorder.

Some people with a form of social phobia called performance phobia have been helped by beta-blockers, which are more commonly used to control high blood pressure. Taken in low doses, they control the physical manifestation of anxiety and can be taken before a public performance.

A novel treatment approach has recently been developed as a result of translational research. It has been shown that a combination of acute dosing of d-cycloserine (DCS) with exposure therapy facilitates the effects of exposure therapy of social phobia (Hofmann, Meuret, Smits, et al., 2006). DCS is an old antibiotic medication used for treating tuberculosis and does not have any anxiolytic properties per se. However, it acts as an agonist at the glutamatergic N-methyl-D-aspartate (NMDA) receptor site, which is important for learning and memory (Hofmann, Pollack, & Otto, 2006). It has been shown that administering a small dose acutely 1 hour before exposure therapy can facilitate extinction learning that occurs during therapy.

Treatment controversy arises because while some studies indicate that a combination of medication and psychotherapy can be more effective than either one alone, others suggest pharmacological interventions are largely palliative, and can actually interfere with the mechanisms of successful therapy. Meta-analysis indicates that psychotherapeutic interventions have better long-term efficacy compared to pharmacotherapy. However, the right treatment may very much depend on the individual patient's genetics and environmental factors.

### **Alternative medicine**

Regular aerobic exercise, improving sleep hygiene and reducing caffeine are often useful in treating anxiety.

Herbal drugs are often used in patients with somatoform disorders. In one clinical trial, butterbur in a fixed herbal drug combination (Ze 185 = 4-combination versus 3-combination without butterbur and placebo) was used in patients with somatoform disorders. For a 2-week treatment in patients with somatization disorder (F45.0) and undifferentiated somatoform disorder (F45.1), 182 patients were randomized for a 3-arm trial (butterbur root, valerian root, passionflower herb, lemon balm leaf versus valerian root, passionflower herb, lemon balm leaf versus placebo). Anxiety (visual analogue scale - VAS) and depression (Beck's Depression Inventory - BDI) were used as primary parameters, and Clinical Global Impression (CGI) was used a secondary parameter. The 4-combination was significantly superior to the 3-combination and placebo in all the primary and secondary parameters (PP-population), without serious adverse events.

Many other natural remedies have been used for anxiety disorder. These include kava, where the potential for benefit seems greater than that for harm with short-term use in patients with mild to moderate anxiety. Based on Cochrane's systematic review of seven RCTs (n = 380), with findings

supported by five lower-quality trials (n = 320), the American Academy of Family Physicians (AAFP) recommends use of kava for patients with mild to moderate anxiety disorders who are not using alcohol or taking other medicines metabolized by the liver, but who wish to use "natural" remedies. Side effects of kava in the clinical trials were rare and mild.

Inositol has been found to have modest effects in patients with panic disorder or obsessive-compulsive disorder. St. John's wort and Sympathyl have also been used to treat anxiety, but with little scientific evidence as to their effectiveness.

### **Epidemiology**

In the United States the lifetime prevalence of anxiety disorders is about 29%.

### **Prognosis**

It is the most common cause of disability in the workplace in the United States.