



AMERICAN COLLEGE OF
OCCUPATIONAL AND
ENVIRONMENTAL MEDICINE

Anxiety Disorders

Effective Date: April 30, 2021

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Summary of Recommendations

The following summary table contains recommendations for evaluating and managing Anxiety Disorders from the Evidence-based Workplace Mental Health Panel. These recommendations are based on critically appraised higher quality research evidence or, when such evidence was unavailable or inconsistent, on expert consensus as required in ACOEM's Methodology.

Recommendations are made under the following categories:

- Strongly Recommended, "A" Level
- Moderately Recommended, "B" Level
- Recommended, "C" Level
- Insufficient – Recommended (Consensus-based), "I" Level
- Insufficient – No Recommendation (Consensus-based), "I" Level
- Insufficient – Not Recommended (Consensus-based), "I" Level
- Not Recommended, "C" Level
- Moderately Not Recommended, "B" Level
- Strongly Not Recommended, "A" Level

Anxiety Disorders Screening Tools	Moderately Recommended, Evidence (B)
Psychometric Testing: Anxiety Disorders	Moderately Recommended, Evidence (B)
Pharmacogenomics Testing	No Recommendation, Insufficient Evidence (I)
Education	Recommended, Insufficient Evidence (I)
Aerobic Exercise	Moderately Recommended, Evidence (B)
Strengthening Exercise	Recommended, Insufficient Evidence (I)
Flexibility-Based Exercise	Not Recommended, Evidence (C)
Yoga	Recommended, Insufficient Evidence (I)
Cognitive Behavioral Therapy	Moderately Recommended, Evidence (B)
Computer-Assisted Cognitive Behavioral Therapy	Moderately Recommended, Evidence (B)
Bibliotherapy/Cognitive Behavioral Therapy Bibliotherapy	Recommended, Evidence (C)
Dialectical Behavior Therapy	No Recommendation, Insufficient Evidence (I)
Acceptance and Commitment Therapy	Moderately Recommended, Evidence (B)
Interpersonal Therapy	Recommended, Insufficient Evidence (I)
CBT with Antidepressants	Moderately Recommended, Evidence (B)
Insight-Oriented Therapies (Including Short-Term Psychosocial Psychotherapy)	Recommended, Insufficient Evidence (I)
Stress Inoculation Training	No Recommendation, Insufficient Evidence (I)
Stress Management (Behavioral, Cognitive, or Physical)	No Recommendation, Insufficient Evidence (I)
Supportive Therapy	No Recommendation, Insufficient Evidence (I)
Distractive Methods	Recommended, Evidence (C)
Exposure Therapy and Prolonged Exposure Therapy	Recommended, Insufficient Evidence (I)
Virtual Reality Exposure Therapy	Recommended, Insufficient Evidence (I)
Meditation, Mindfulness, and Relaxation	Recommended, Insufficient Evidence (I)
Emotional Freedom Therapy	No Recommendation, Insufficient Evidence (I)
Antidepressants	Moderately Recommended, Evidence (B)

Benzodiazepines, Routine Use	Not Recommended, Evidence (C)
Benzodiazepines, Select Use	Recommended, Evidence (C)
Buspirone	Recommended, Evidence (C)
Antipsychotics (Quetiapine)	Moderately Recommended, Evidence (B)
Beta-Blockers: Propranolol, Atenolol	Moderately Recommended, Evidence (B)
Gabapentin	No Recommendation, Insufficient Evidence (I)
Pregabalin	Moderately Recommended, Evidence (B)
Valproic Acid	No Recommendation, Insufficient Evidence (I)
Antihistamine (Hydroxyzine)	Recommended, Evidence (C)
Nutraceuticals	No Recommendation, Insufficient Evidence (I)
St. John's Wort (Hypericum Perforatum)	Not Recommended, Evidence (C)
Kava Extract	No Recommendation, Insufficient Evidence (I)
Lavender Oil	No Recommendation, Insufficient Evidence (I)
Valerian	Not Recommended, Evidence (C)
Marijuana, Cannabis, Cannabinoids, and Cannabidiol	Not Recommended, Insufficient Evidence (I)
Transcranial Magnetic Stimulation and Repetitive Transcranial Magnetic Stimulation (rTMS)	No Recommendation, Insufficient Evidence (I)
Brainwave Synchronization	No Recommendation, Insufficient Evidence (I)
Acupressure	No Recommendation, Insufficient Evidence (I)
Acupuncture	Not Recommended, Evidence (C)
Massage	No Recommendation, Insufficient Evidence (I)
Therapeutic Touch	No Recommendation, Insufficient Evidence (I)
Physical Medicine Treatment	No Recommendation, Insufficient Evidence (I)
Benzodiazepine Discontinuation and Tapering	Recommended, Evidence (C)
Pregabalin for Benzodiazepine Tapering and Discontinuation	Recommended, Evidence (C)
Odansetron for Benzodiazepine Tapering and Discontinuation	Not Recommended, Evidence (C)
Electroacupuncture for Benzodiazepine Tapering and Discontinuation	Not Recommended, Evidence (C)

Related Terms

- Anxiety
- Anxiety Attack
- Generalized Anxiety Disorder
- Phobia
- Phobic Disorders
- Social Anxiety Disorder
- Panic Disorder
- Panic Attack
- Agoraphobia
- Substance/Medication-Induced Anxiety Disorder
- Adjustment Disorder with Anxious Mood

Introduction

Anxiety disorders are the most prevalent mental health conditions, particularly in many western societies, and the burden of these conditions is often unclear or underestimated [1, 2]. Even in affluent countries with developed health systems, there is evidence that most anxiety disorders go unidentified and thus are unaddressed by healthcare providers. More than half of individuals diagnosed with an anxiety disorder suffer from more than one such condition, illustrating the highly co-morbid nature of this group of disorders [1]. Furthermore, the capacity to effectively address these conditions is undermined by a dearth of effective prevention methods as compared with other mental health disorders, which is potentially a reflection of the chronic nature of this condition, particularly when the anxiety goes untreated [1]. Thus paradoxically, the pervasive nature of these anxiety disorders both emphasizes the need for effective mitigation, identification, and treatment of these conditions and undermines efforts toward this goal.

Anxiety disorders (including separation anxiety disorder, selective mutism, specific phobia, social anxiety disorder, panic disorder, agoraphobia, and generalized anxiety disorder) affect approximately 40 million Americans (18.1%) each year [1, 3]. Findings from the World Mental Health Survey Initiative in 2007 indicate that approximately one out of every four individuals has historically suffered from or are likely to develop an anxiety disorder [4]. The lifetime prevalence estimates for anxiety disorders vary by country, with the rate in the United States estimated to be approximately 33% [1, 5, 6]. The prevalence of anxiety disorders is reportedly higher in high-income countries; 12-month prevalence rates in the United States and Europe tend to be elevated when compared with other regions [7]. As with other mental health disorders, culture-bound manifestations of anxiety have been identified; however, Creske [1] noted that “determining the extent to which these are unique categories or cultural variations of a common pathology is challenging.”

Although some risk factors associated with a shift from adaptive to dysfunctional anxiety are linked with a singular anxiety disorder or set of symptoms, others convey a vulnerability to developing an anxiety disorder more broadly. Family history of anxiety or depressive disorders and female gender are associated with increased risk of developing all anxiety disorders [1, 8-11]. Anxiety disorders are twice as common among females [1]. Children of individuals diagnosed with one or more anxiety disorders are two to four times more likely to develop an anxiety disorder during their lifetimes. Interestingly, parental history of depression and anxiety exacerbated the risk of offspring anxiety, indicating that a family history of depression independently presents a vulnerability for anxiety in subsequent generations [12]. Additional risk factors for anxiety disorders include insomnia [13] and chronic diseases [9, 14]. Multiple personality factors are predictors for anxiety disorders, including low self-esteem, high neuroticism, low extraversion, low conscientiousness, and timid social behavior [8, 15, 16].

The financial impact of these disorders is evident in statistics that have identified anxiety disorders as the sixth leading cause of disability worldwide [1, 17, 18]. Anxiety disorders

affecting more than 60 million Europeans cost more than 74 billion euros, largely due to indirect costs such as disability [19, 20]. However, the human health cost of anxiety disorders goes far beyond these statistics. Anxiety symptoms have been shown to be associated with cardiovascular events [21-25], joint and muscle pain [26], chronic pain [27], gastroenteritis [28], and cannabis dependence [29].

The interaction between anxiety disorders and substance use is complex; smoking and alcohol abuse have been identified as risk factors for anxiety disorders, as well as being associated with bidirectionality [30]. Similarly, depression has been identified as a risk factor for anxiety [31]. In longitudinal studies, the reverse has been demonstrated: the presence of any anxiety disorder is associated with an increased risk of depressive disorders [32].

Anxiety disorders can have meaningful impacts among occupational populations. In 2006, an Anxiety Disorders Association of America survey found an estimated prevalence of anxiety disorders among US workers of 9.0% [3]. Among the affected employees, 72% reported that their daily anxiety interferes with their lives moderately, 40% reported that they experience excessive anxiety on a daily basis, and 28% reported that they have had an anxiety or panic attack [3]. In addition, 30% reported that they take prescription medication to manage stress, nervousness, emotional problems, or lack of sleep [3]. Data suggest that anxiety disorders are associated with quality of work, workplace performance, and relationships among coworkers and superiors [3]. Poor job productivity is associated with anxiety disorders, as well as short-term and long-term disability [33-36].

Anxiety is among the most common of all mental health disorders. Anxiety has a number of subtypes, including generalized anxiety disorder, panic disorder, agoraphobia, specific phobias, social anxiety, and other conditions. Studies related to the topic of anxiety may not define the manner in which this term is being used, as the term “anxiety” is often used interchangeably with what would more precisely be termed *anxiety disorder(s)* or *anxiety symptoms*. Complicating matters further, there are terminology and criteria differences between the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), International Classification of Diseases, Tenth Edition (ICD-10), and International Classification of Diseases, Eleventh Edition (ICD-11) nomenclatures. In addition, review studies may combine articles that define “anxiety” as a GAD-7 score above a cutoff point with studies that use more specific criteria, such as a formal diagnostic interview and formal criteria.

The defining characteristics of anxiety disorders include excessive and persistent anxiety and fear, often accompanied by avoidance of perceived threats. The threats that are the source of the anxiety can be internal (bodily sensations) or external (specific circumstances or triggers such as heights and social situations). Avoidance is a common feature of many anxiety disorders, as are panic attacks [1].

A number of specific anxiety diagnoses fall under the umbrella of anxiety disorders. These categories of anxiety are included in both the DSM-5 and the ICD-10. The diagnostic criteria for

specific anxiety diagnoses are largely consistent across both classification systems. However, it should be noted that the DSM-5 diagnostic classification has not been incorporated by most currently available epidemiological studies [1].

The classification of anxiety disorders in the DSM-5 presumes that anxiety disorders are independent and discrete from one another, despite the fact that there is both a high level of symptom overlap between various anxiety diagnoses as well as notable symptom variation with a single diagnosis [2]. DSM-5 anxiety disorder categories include the following: separation anxiety disorder, selective mutism, specific phobia, social anxiety disorder, panic disorder, agoraphobia, generalized anxiety disorder, substance/medication-induced anxiety disorder, anxiety disorder due to another medical condition, other specified anxiety disorder, and unspecified anxiety disorder.

In contrast with previous versions of the DSM, posttraumatic stress disorder (PTSD) and obsessive-compulsive disorder were re-assigned to chapters distinct from the anxiety disorders listed above in the DSM-5. A complete listing of the diagnostic categories and criteria in use in the DSM-5 are described later in the guideline [37, 38]. The ICD-10 diagnostic criteria are more commonly used outside of the United States.

While the clinical presentations of the various subtypes of anxiety have similarities, their etiologies may differ. Similarly, available treatments for anxiety are highly divergent, and yet a number of these diverse treatments have been shown to be effective. Consequently, numerous subtypes of anxiety have been defined [37, 39-41], and the origins of anxiety have been attributed to a number of underlying mechanisms. Three of the most important of these are the evolutionary, biological, and cognitive models.

Origins of Anxiety

Anxiety as an Evolutionary Survival Mechanism

Evolutionary theory is the central theory of biology, and it has been stated that no other diagnosable psychological condition is more closely aligned with evolutionary principles than is anxiety [42, 43]. From the standpoint of evolutionary theory, the emotional states of anxiety, fear, and anger play a central role in defensive strategies that help humans to survive. According to this theory, although anxiety, fear, and anger are all associated with the increased arousal in the sympathetic nervous system, each emotional state channels this survival energy differently. Anger involves a behavioral attempt to eliminate a threat, whereas fear is associated with attempts to escape a known immediate threat to one's welfare [44]. Both aggression and escape behaviors are associated with intense exertion. Intense fear such as that seen in phobias often manifests with symptoms such as elevated heart rate, shortness of breath, and sweating, preparing the individual for the intense aerobic activity needed to cope with a threat. In contrast to fear and anger, anxiety involves increased vigilance for vague or potential threats; it may be more likely to manifest in the form of cognitive worrying, rumination, or hypervigilance. Because fear and anger are associated with the perception of an

objective threat, they are more likely to resolve when the threat is no longer present. In contrast, because anxiety pertains to potential threats, it may be less likely to resolve. Overall, anxiety, fear, and anger differ with regard to the nature of the threat and type of response, but the mechanisms of sympathetic arousal observed in these emotional states are very similar [44].

In some contexts, fear and anxiety are adaptive and facilitate self-protective behaviors. As described previously, it has been theorized that the function of anxiety is to increase vigilance so as to improve threat detection in the environment. Thus, to the degree that an individual's level of anxiety is based on an accurate estimate of the level of environmental threat, anxiety is adaptive and promotes survival and welfare [43]. From the evolutionary perspective, anxiety could be conceptualized as a cognitive strategy of "erring on the side of caution" that persists until the individual is convinced that the environment is safe [45].

In other cases, though, if cognitive estimates of the level of threat grossly exceed what is objectively present in the environment, a psychological disorder results. If overestimates of a specific threat lead to excessive fear (e.g. after one motor vehicle accident, believing horrible accidents are inevitable and reacting with terror), the condition is called a phobia. In contrast, if vague potential threats are overestimated (e.g. excessive worries that physicians have failed to identify an unknown but serious medical condition), the condition is called anxiety [44]. Maladaptive anxiety is sustained by inaccurate cognitions that overestimate the level of threats that are present, and can persist even if the individual exists in an environment where threats are highly unlikely [46]. Exaggerated or "catastrophized" cognitions result in a tendency to focus excessive attention on scanning for potential threats, overestimating ambiguous situations as threatening, and reacting to perceived threats with disproportionate levels of anxiety [47].

Fight-or-Flight Response and the General Adaptation Syndrome

The fight-or-flight response is an evolutionary-based instinctual survival strategy present in mammals and other life forms. Cannon theorized that upon encountering a threat, the fight-or-flight response empowers the organism to engage the survival strategies of either aggression to eliminate the threat, or fleeing to escape the threat [48]. Although the fight-or-flight response is currently most closely associated with anxiety [49], Cannon's original theory was equally a theory of aggression, which emphasized that anxiety and anger are linked as survival strategies [48].

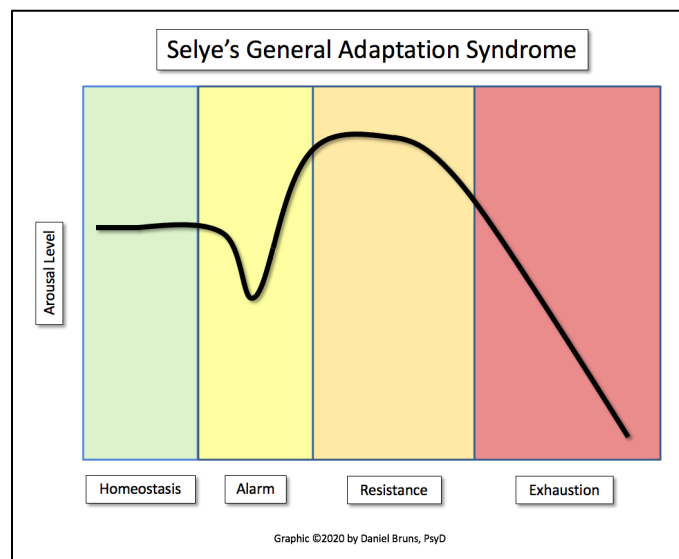
Cannon's concept of fight or flight influenced Selye's research on the general adaptation syndrome (GAS). Selye's model expanded our understanding of the biological mechanisms underlying anxiety, as well as the physiological effects of long-term stress [50]. Selye conceived of the fight-or-flight response more broadly as a syndrome developing over time across three stages, and then conducted research showing the impact of this syndrome on health. The three stages of the GAS are as follows:

1. The first stage of GAS consists of a shock reaction that disrupts the organism's homeostasis. Initially, stage 1A involves decreased resistance by the organism, which

may include circulatory shock and syncope or fainting. This is typically a very brief reaction, followed by Stage 1b of the GAS which is the initiation of a fight-or-flight type of response, where the organism transitions to an aroused physiological state to facilitate self-defense.

2. If the threat is not immediately resolved, the organism enters the second stage of GAS, which is resistance. In this stage, the organism actively produces glucocorticoids such as cortisol and exhibits continuing signs of physiological arousal, while the organism strives to overcome the threat using various means as long as its stamina allows.
3. In the third stage of GAS, the stress response can resolve in one of two ways. First, if the attempts to cope with the threat are successful, the organism can enter a stage of recovery; after a sufficient period of rest, it can return to a normal state of homeostasis. However, if the threat situation does not resolve, the organism will eventually deplete its resources, enter a state of exhaustion, and become symptomatic [50].

Overall, these models depict environmental stresses as part of life. In response to stress, the fight-or-flight response is an adaptive biological mechanism that energizes the organism to rise to the occasion to cope with the onset of a stressor to preserve life and health. Beyond this, Selye's work on GAS then explored the effects of a chronically activated fight-or-flight response. Selye's work pointed out that when stress becomes chronic, the organism's adaptive capacities will eventually become exhausted. At this point, bodily functions may become impaired, and stress-related symptoms will likely appear in the organism's most vulnerable organ system [50, 51]. Metaphorically, GAS posits that a combination of genetic vulnerability, prior injury, and prior disease creates a vulnerable "weakest link" in the bodily system. Under sustained stress, the bodily system that constitutes the "weakest link" is the one most likely to become symptomatic. Thus, GAS helps to explain the relationship between anxiety, physiological arousal, and stress-related disease states: In response to the perception of chronic perceived threat, the organism expends an unsustainable level of energy in the interest of preserving short-term survival, ultimately at the expense of long-term health. In this manner, psychological stresses can be "somatized."



Polyvagal Theory and the Fight, Flight, or Freeze Response

Polyvagal theory was developed by Porges. It contends that the fight-or-flight response is an oversimplification of autonomic activity, because it focuses on the sympathetic component of the autonomic nervous system [52, 53]. Polyvagal theory contends that while the autonomic arousal seen in a stress response is associated with the sympathetic nervous system, ongoing arousal is regulated by parasympathetic circuits in the vagus nerve. This theory holds that evolutionary processes have equipped humans with three vagal parasympathetic circuits that fall along a spectrum in terms of level of response sophistication. From an evolutionary phylogenetic perspective, listed from most sophisticated to most primitive, these three circuits involve social communication, fight or flight, and freeze responses.

Polyvagal theory applies the Jacksonian principle of dissolution to the stress response [54], which would predict that attempts to cope with stress will become less sophisticated over time. Using this principle, Polyvagal theory contends that humans are born with a hierarchy of biological coping mechanisms that are associated with vagus nerve circuits [55, 56]. Under safe circumstances, humans use their most sophisticated methods of problem solving (those that are phylogenetically “higher”), which involve social interactions and communication. The principle of dissolution states that these more advanced (“higher”) brain circuits suppress less advanced (“lower”) circuits. However, the principle of dissolution states that should the more advanced coping strategies fail, the only biological strategies that remain are less effective, more primitive approaches. Thus, when communication fails, the next lower strategy involves activating circuits that regulate the fight-or-flight response. Should the fight-or-flight strategy fail, this in turn is followed by the phylogenetically most primitive circuits contained within our “lizard” brain—the freeze response [55, 56].

Polyvagal theory contends that when communication fails to adequately address a perceived threat, the individual may choose to fight, run away, or freeze in place. Freezing is more likely to occur when a threat is perceived as overwhelming, and neither talking, fighting, nor running away appear to be viable options. For example, if the night clerk in a convenience store is accosted by a robber with a gun, the victim could alternately attempt to persuade the robber to leave, run away, or fight back. However, if none of these strategies are viable options, the final alternative may be to “freeze.” If the anxiety is severe enough, the individual may faint—and in so doing, reduce any perception that they pose a threat to the attacker, potentially generating the best chance for survival [57, 58].

In the clinical setting, the fight-or-flight response is closely associated with anxiety—and in more extreme forms with phobias, panic, and PTSD. In contrast, the freeze response is associated with what could at first glance be mistaken for extreme stoicism, while closer examination may reveal severe distress involving dissociation and emotional numbness characteristic of acute stress disorders. Overall, polyvagal theory has deepened our understanding of the stress response. It also has clinical applications for diagnosis and treatment, such as the use of heart rate variability as a means of assessing parasympathetic activity in the vagus nerve and heart rate variability biofeedback as a treatment to manage autonomic arousal [59].

Monoamine Theory and Anxiety as Disease

While evolutionary theory as above views anxiety disorders as caused by the overactivation of a fear response which is otherwise adaptive, monoamine theory conceptualizes anxiety as a disease resulting from an imbalance of monoamine neurotransmitters. Anxiety and fear symptoms (e.g., panic, phobias) are regulated by an amygdala-centered circuit and by a cortico-striato-thalamo-cortical (CSTC) loop [60]. Additionally, a forebrain region called the bed nucleus of the stria terminalis (BNST) may play an important role in the development of anxiety disorders [61-63]. These circuits may be involved in all anxiety disorders, with the different anxiety conditions reflecting not different circuitry within the brain, but rather divergent forms of dysregulation within those circuits [60, 64-66]. Dysregulation in these circuits is thought to be associated with aberrant levels of monoamine neurotransmitters [66-69], and could be associated with a disease process or genetic predispositions to an anxious temperament. Studies have found that anxious temperament may be heritable and associated with dysregulation in fronto-limbic brain circuits [62]. A twin study by Davies in 2015 estimated that 42% of the variance in generalized anxiety was attributable to genetics.

Anxiety is known to be highly comorbid with depression [70]. Anxiety and depression share the symptoms of arousal/agitation, sleep, fatigue, and concentration difficulties. However, while anxiety is associated with fear and worry, depression is more closely associated with anhedonia and loss of interest.

Although anxiety and fear play a valuable role in survival, the role played by [depression](#) in survival and coping is less clear but may involve helping the individual to relinquish impossible goals. Despite the differences in anxiety and depression, both are associated with a history of negative life experiences, difficulty regulating emotions, and fronto-limbic brain circuits regulated by serotonin [67]. Other studies have also associated anxiety with levels of dopamine [66] and GABA [68, 69], and have observed that anxiety has a paradoxical relationship with norepinephrine [71]. That is, although there is a strong correlation between anxiety and elevated levels of norepinephrine in the bloodstream, medications that increase levels of norepinephrine in the synapse paradoxically alleviate anxiety [71]. Because anxiety has been found to respond to treatments increasing levels of monoamine neurotransmitters (e.g., serotonin, norepinephrine, and dopamine), monoamine theory applies to anxiety as well as depression. Other studies have also suggested that social anxiety may be alleviated by alcohol [72] and separation anxiety by opioids [73]. Overall, from a clinical perspective, the findings of pharmaceutical treatments for anxiety have primarily focused on the serotonin system, making serotonin a first-line treatment of anxiety [66] and monoamine dysregulation a primary method of explaining anxiety disorders [71, 74].

Anxiety as a Cognitive Disorder

A third influential theory of the origin of anxiety is cognitive theory. Cognitive theory holds that emotional and behavioral problems are due to incorrect or maladaptive ways of thinking, including distorted perceptions of oneself, others, and environmental circumstances [75-77]. In

contrast to the monoamine hypothesis, which describes the origins of anxiety and depression in biological terms, cognitive theory holds that anxiety and depression have their origins in thought. Although depression is believed to be most closely associated with helpless/hopeless thinking, anxiety is more closely associated with catastrophic thinking that overemphasizes the seriousness of one's circumstances [60]. Similar to evolutionary theory, cognitive theory would hold that while anxiety and fear may have a valid purpose, anxiety and phobic disorders result when distorted cognitions grossly overestimate the objective level of threat, and in so doing dysregulate the anxiety/fear system. Unlike evolutionary theory, however, the cognitive theory of anxiety does not hypothesize an evolutionary origin. Instead, the cognitive theory of depression and anxiety has been characterized by Beck as an "information processing model" [75, 78] that was influenced by other cognitive theorists such as Piaget and Kelly [79, 80].

Cognitive theory hypothesizes that behavior is guided by cognition, and that many cognitive processes, once learned, become habitual or "automatic" [75]. In some cases, these cognitions are helpful to enable the individual to accurately perceive and automatically respond to events in the environment [75], making it possible to "multitask." In other cases, over the course of an individual's history of interacting with the environment, the individual's cognitive processes may become biased or distorted. This can in turn lead to distorted perceptions, and to dysfunctional behavior, depression and anxiety [75, 81]. Because cognitions often occur in a rapid and automatic manner, the individual may not be explicitly aware of cognitions or the distorted perceptions created by these thoughts.

Cognitive theory has also inspired therapies for anxiety [76]. Perhaps the most noteworthy of these is Beck's system of cognitive therapy. Beck's therapeutic approach to anxiety involves the process of examining cognitions related to anxiety and replacing those that are distorted or dysfunctional (e.g., catastrophizing [82-86] or kinesiphobia [87-89]) with cognitions that are accurate and more functional [90, 91]. CBT could thus be said to involve something akin to the scientific method. In essence, the patient is taught to identify automatic cognitions, test the accuracy with which these hypothesized beliefs portray reality, and determine the degree to which they enable effective coping. The objective of cognitive behavioral therapy is to identify any faulty or distorted cognitions and replace them with more adaptive ones. A weakness of CBT is that, because it often involves a process of journaling about thoughts and feelings, it is in essence "thinking about how you think," and many such protocols require at least an average level of literacy. Recently, however, low-literacy versions of cognitive therapy have been developed [92].

Cognitive processes are also closely associated with behavior. It has been observed that perceptions of threat leads to avoidance of the threatening object. If the perceptions of threat are exaggerated though, the individual has no opportunity to unlearn them since the threaten object is avoided [93, 94]. To address pathological avoidance, behavior therapists developed nonintrospective therapeutic techniques such as exposure therapy [95]. In exposure therapy, the patient with exaggerated or phobic anxiety is exposed to the phobic object for a prolonged period. When the feared event does not happen, the anxiety is extinguished [96, 97].

Over the course of time, these disparate cognitive and behavioral therapeutic techniques were determined to be synergistic, and were aggregated into “cognitive behavioral therapy” or CBT. It has been observed by Beck that CBT has become the accepted generic umbrella term used to classify various combinations of these cognitive and behavioral techniques [78].

Attempts have been made to reconcile cognitive theory and CBT methods with biological models of anxiety. One such framework applied the diathesis-stress model to emotional disorders, hypothesizing that adverse childhood experiences may create a vulnerability to emotional disorders in adulthood. Later in life, if a vulnerable individual copes with environmental stressors using dysfunctional beliefs and maladaptive coping strategies, emotional disorders may result [98, 99]. Consistent with this hypothesis, studies have suggested that the effectiveness of CBT could be associated with reduced activation of the amygdala and hippocampal regions of the brain [98], and that CBT treatment may promote positive changes in brain functioning in the anterior cingulate cortex, the posterior cingulate, and the prefrontal cortex [100].

Stay at Work / Return to Work

Stay at work/return to work usually requires analyses and consideration of the diagnoses, severity, personal psychosocial factors, work organizational factors, job strain, treatment, response to treatment, and job factors (e.g., safety-critical work). General discussion regarding psychological conditions and the workplace is discussed in the [Workplace Mental Health Introduction](#). Briefly, there are three considerations: risk, capacity, and tolerance. Risk is whether a job would place someone or their co-workers at risk by being in the work environment. Capacity reflects an, ideally, objective opinion on someone's actual abilities. Tolerance is the person's choice to remain or re-enter the work environment based on the perceived benefits [101]. As favorable and improved health and mental health status have been uniformly shown by stay at work/return to work, it is critical to optimize rather than medicalize these cases and factors.

As with many psychological conditions, there is frequent confusion regarding the presence of a psychological diagnosis and the individual's ability to work. General discussion regarding psychological conditions and the workplace was discussed in the [Workplace Mental Health Introduction](#). Laypeople and professionals alike have misperceptions regarding individuals who have psychological conditions.

Generally, many professionals express uncertainty about whether an individual with an anxiety disorder can work [37, 102-105]. Frequently, once a psychological diagnosis is identified, the diagnosis alone may be utilized by both the individual with the condition as well as treating professionals as the primary reason for indicating that the person cannot work [37, 102-104, 106-116]. However, empirical research consistently demonstrates that the presence of an anxiety disorder, like the majority of mental health conditions, is not sufficient to indicate the presence of impairment in functioning because the majority of people with these types of

psychological conditions continue to work [103, 104, 108-112, 114-118]. Importantly, employment is found to have a profound positive health benefit on physical and mental health [106]. This is true with anxiety disorders as well. The positive benefits of work and the role an individual has in the workplace play a role in enhancing mental health well-being.

However, some patients mistakenly believe that avoidance of exposure to any triggers that may cause anxiety is the most appropriate and effective strategy to avoid experiencing anxiety, because it may work temporarily in reducing anxiety. However, this perception is inaccurate. Instead, the person with anxiety tends to experience further reductions in social interaction and involvement in most activities. This results in the person with anxiety experiencing progressively greater limitations of ordinary activities and events when the individual gradually becomes anxious in more situations. Moreover, because the individual tends to experience anticipatory anxiety (e.g., thinking about an anxiety-triggering situation and experiencing anxiety without direct exposure to the situation), this further confirms to the individual that the anxiety is affecting the ability to function in normal life activities, such as socializing and working. It also gives the erroneous impression of the anxiety occurring continuously. This is because the individual becomes more and more vigilant about experiencing *any* anxiety, rather than just the anxiety related to specific situations and events [119-121].

This combination of both anticipatory anxiety and the avoidance of any direct exposure to specific triggers plays a role in maintaining internalized anxious self-talk. In essence, the person now believes that any anxiety is a sign that the anxiety is uncontrolled. Much as with internalized self-talk that occurs with individuals with depressive disorders, the same process occurs with individuals with anxiety conditions. The person becomes focused on a continual assessment of whether any anxiety is occurring. The person learns to fear any sense of anxiety. Although anxiety plays a role in keeping safe from harm and in recognizing potential threats to safety, most individuals with anxiety conditions overestimate the probability of harm. Because of this, a person with an anxiety disorder perceives potential of serious harm, even where none realistically exists. Frequently, individuals with anxiety conditions are not able to effectively filter valid safety threats from those low-level issues. Instead, all potential threats are viewed as safety threats, whether valid or not, and result in the person remaining vigilant to avoiding harm through avoidant behaviors. The person becomes preoccupied with self-protection on all levels, not solely the original triggering event for anxiety. Ultimately, the individual becomes intolerant of uncertainty [122-128].

It is the vigilant behavior that remains constant and keeps an individual in a heightened state of physical arousal (e.g., increased heart rate, increased rate of respiration, increased muscular tension, reduced ability to maintain focus on mental and physical activities). In other words, the individual frequently may report being unable to relax completely both physically due to heightened physical arousal and mentally due to the ongoing vigilance regarding experiencing anxiety.

Empirical research consistently demonstrates that individuals with anxiety disorders reduce and avoid exposure to situations, people, or events only serve to increase anxiety further. Thus, the perception of avoiding the things that cause an individual to become anxious becomes increasingly self-limiting and, in the long-term, more ineffective because the individual continues to experience anxiety.

Frequently, individuals with anxiety conditions report that the experienced anxiety is sustained/continuous on a daily basis. However, with careful assessment as well as having the individual track when anxiety occurs, what is usually found is that the individual has periods of time where anxiety is not occurring. The person may become distracted in doing an activity, such as watching television or talking with another individual. This is also helpful in gaining a sense of what is actually occurring during a typical day for the individual with anxiety. Moreover, most individuals continue to complete activities of daily living, including self-care, caring for others, household tasks, paying bills, driving, and working, despite experiencing anxiety. These are important points to consider as part of the evaluation of any reported perceived impairment in functioning related to anxiety.

It is essential that the subjective perceptions held by individuals with an anxiety condition as well as treating professionals are addressed as part of the assessment and treatment process. In addition to evaluating the individual, the use of standardized psychological testing to confirm or rule out the presence of an anxiety disorder as well as the purported severity of it are more objectively assessed [129-133]. The importance of standardized psychological testing is discussed in depth in the [Workplace Mental Health Introduction](#).

It is imperative that the professional who is evaluating the individual with a potential anxiety condition refrain from medicalizing normal behavior. Medicalization occurs when either an individual who is experiencing a potential anxiety condition or the professional inappropriately take normal behaviors and indicates that the behaviors are related to a potential condition. Frequently, this occurs when an individual or professional takes symptoms as evidence that a condition is occurring versus determining this in a systematic manner using both specific diagnostic criteria and psychological testing. Symptoms alone are not evidence of a psychological condition.

In addition, the current evidence-based treatments for anxiety disorders focus on addressing the person's internalized anxious self-talk and developing tools to refute. In addition, as part of the treatment process, it is essential to discuss and educate those with anxiety disorders who seek a request for workplace absence or long-term workplace accommodations about the goals of staying at work or returning to work. It is essential for professionals to address misperceptions immediately in the evaluation and treatment processes. This serves to keep the individual engaged in appropriate personal and workplace activities. More specific information regarding current psychological treatments that address anxious behavior regarding the workplace are described in this section.

Common Issues with Determining Potential Impairment in Functioning

In this section, the presence of potential and diagnosed anxiety disorders and the individual's functional capacity related to staying at work (SAW) or returning to work (RTW) are examined in greater depth.

It is essential to note some common misperceptions pertaining to anxiety disorders. Laypersons and professionals alike tend to perceive the presence of an anxiety disorder to be the same as having a reduced capacity to work based simply on the presence of the diagnosis of anxiety disorder. However, just as physical conditions do not necessarily equate to work incapacity, the same is true for psychological conditions. Most individuals with a mental health condition continue to work. Thus, if a person is said to have ongoing impairment in functioning with an anxiety disorder, this is unusual and should be further evaluated to confirm or rule out whether impairment in functioning objective exists and is not based on the individual's perceptions alone.

Second, professionals frequently either do not define the severity of a diagnosed anxiety disorder or simply report that the identified anxiety disorder is severe. This is a critical point regarding anxiety disorders, because most symptoms related to the identified anxiety condition are not consistently present throughout the day or even throughout the week or month. Because of this, it is unlikely that an individual will experience a sustained severe anxiety disorder. Consequently, it is unusual for a professional to report that an individual experiences a severe anxiety disorder accompanied by sustained impairment in functioning. This requires further evaluation to determine the true extent of any reports of severe anxiety that affects functioning. Instead, because the person reports that anxiety still occurs regularly, both the person and the professional believe that is the basis for determining purported severity of an anxiety disorder.

Moreover, there is a great deal of variability in how individuals experience anxiety symptoms. The triggers for one individual's anxiety condition are not necessarily the same for another person. Because of this, it is critical to utilize the diagnostic criteria specific to each anxiety disorder. The diagnostic criteria provide guidance regarding the required time span during which anxiety occurs, and the types and number of diagnostic criteria that must be met in order to make the diagnosis of each anxiety disorder. Although variability in the type of triggers may differ from individual to individual, the primary diagnostic criteria do not. Frequently, professionals simply note "anxiety" or "severe anxiety" without consideration of diagnostic criteria when indicating that an individual cannot work. However, in order to know which anxiety disorder is occurring, the diagnostic criteria must be followed and noted as part of the evaluation process of anxiety disorders.

Physiologically, both men and women have the same stress response circuitry regarding the limbic system and its activation. However, there are some differences between how men and women experience anxiety [134-145]. For example, men tend to experience greater conditioned fear response. Men differ from women in how fear develops (fear acquisition)

[138-147]. Importantly though, men and women do not differ in how they learn to extinguish fear, when learning techniques to stop the anxiety response [136, 137, 146]. Women, in general, are at higher risk of developing anxiety disorders. In addition, women may experience anxiety during different phases of their reproductive lives, such as menses, pregnancy, and menopause [147-158]. Frequently, these gender differences are not considered in providing treatment of anxiety disorders.

The importance of differentiating between the severity of anxiety disorders is essential so that the confirmation or ruling out of impairment in functioning is much clearer. Moreover, the identification of psychosocial issues must occur as well, so that problematic issues that negatively impact on both staying at work and returning to work are addressed [159]. Although ruminative thoughts are present with anxiety disorders, these types of thoughts must be separated from psychosocial issues, such as job dissatisfaction, workplace conflict, and job demands [160, 161].

To illustrate this more clearly, the severity of the anxiety disorder conditions varies a great deal from one condition to other. For example, Adjustment disorder with anxious mood is generally less severe than Generalized anxiety disorder. Generalized anxiety disorder varies in severity from mild or moderate to severe. Tables 1 and 2 provide recommendations to consider for facilitating both the SAW and RTW processes regarding anxiety disorders. Each table has further discussion regarding specific factors to consider for the SAW and RTW.

Moreover, when looking at other types of research, the individual expectations (both positive and negative) are found to exert powerful, pervasive control over the individual continuing to experience anxiety [109, 110]. Other factors, such as biases in affective forecasting of future anxiety experiences, as well as reduction in the person's cognitive and behavioral flexibility, play a substantial role in maintaining anxiety and avoidant behaviors [118, 122-128, 134, 162-164].

In addition, psychosocial issues play a role in individuals seeking workplace absences. The most common workplace psychosocial issues are frequently job dissatisfaction, high work demands, low control within the workplace, workplace bullying, workplace conflict, and lack of balance between personal and work life. Professionals must assess for the presence of psychosocial issues as part of the evaluation and treatment processes to both identify them and to avoid medicalizing them. As noted previously, psychosocial issues frequently impede treatment progress as well as facilitating the individual to SAW or RTW [113, 165-174].

In evaluating and treating anxiety disorders, all of these issues must be further assessed because they play a role in the perceptions of individuals with anxiety as well as professionals. Moreover, it is the combination of these issues that lead to the sustained anxiety, reduced flexibility, and increased avoidant behaviors as opposed to the anxiety disorder itself [102-105, 107-118, 175-181].

Main Anxiety Disorders in the Workplace

Three main anxiety disorders occur in the workplace with the greatest frequency: adjustment disorder, panic disorder (with and without agoraphobia), and generalized anxiety disorder.

Individuals with anxiety disorders frequently experience a decrease in workplace performance. This is an exemplary cause of a phenomenon called “presenteeism.” Presenteeism occurs when a person shows up to work, may have a psychological condition, and generally is not operating at previous levels of productivity. Presenteeism frequently occurs before the individual is diagnosed with an anxiety disorder. It is important to ask individuals during assessment if they have noticed a decrease in their workplace productivity [117, 118, 182-186].

The DSM-5 diagnostic criteria for adjustment disorder with anxiety mood, panic disorder, and generalized anxiety disorder are discussed later in the guideline. A brief discussion of the salient points regarding these anxiety disorders is presented here. It is important to note that these anxiety conditions have overlap in many of the anxiety symptoms that are experienced [37, 187].

Adjustment disorder with anxious mood has emotional and behavioral symptoms that occur related to an identifiable stressor or stressors. Of note, an adjustment disorder typically develops within 3 months of the stressor occurring. It usually lasts no longer than 6 months after the stressor or resulting consequences have stopped. Typically, individuals with Adjustment disorder with anxious mood experience a significant level of anxiety after the stressor occurs. At this point, the individual with this condition may be at increased risk for suicidal attempts. This must be thoroughly assessed. However, over time, the individual’s anxiety decreases as the stressor is terminated and the individual has learned specific techniques to manage anxious thoughts and behaviors. Typically, individuals with adjustment disorder with anxious mood do not require workplace accommodations or workplace absence [37, 188].

With panic disorder, the individual frequently experiences panic attacks. This attack is short-natured in length. Typically, individuals experience intense fear or physical discomfort. This peaks within minutes (e.g., 15-20 minutes). Although the frequency and severity of panic attacks vary a great deal, how the individual experiences the intense fear or physical symptoms is the same. Many individuals with panic disorder develop anticipatory anxiety. That is, the individual begins to fear experiencing anxiety before it even occurs. Many individuals worry because of physical symptoms that they may have cardiac or neurological conditions. They fear being potentially embarrassed by their behavior during panic attacks. These individuals also fear that they may “go crazy” or even lose control. Because of this, individuals with panic disorder frequently begin to withdraw from social interaction. With this withdrawal, the person may experience temporary relief from potential anxiety triggers, but this type of action does not decrease anxiety or help the person to cope in a meaningful way. Instead, treatment focuses on addressing the individual’s sensitivity to anxiety as well as the misperception that anxiety symptoms are a harbinger of harm. It is essential to work with individuals with panic

disorder in developing a SAW or, if on a workplace leave, an RTW plan as a part of the treatment goals [37, 189].

Generalized anxiety disorder (GAD) is characterized by excessive worrying and anxiety about many potential events or situations. The key element associated is that the person's anxiety and worry are out of proportion to the situation or have a misperception of the probability of a negative outcome are grossly overestimated. Frequently, individuals with GAD report that it is difficult to control their anxiety and that they have difficulty in pushing anxious thoughts away. The worries that occur with GAD are excessive. The worry may occur without a specific trigger. Usually, the individual develops a sense of "being wired" or on edge. Importantly, individuals with GAD report constant worry that begins to impact on interaction with others. Thus, the individual expends a great deal of energy throughout the day worrying versus engaging in productive behavior. Sleep issues also contribute to sustained GAD symptoms [37].

With each of these anxiety disorders, there usually is no need to have a workplace absence if the individual is not experiencing suicidal ideation. Moreover, there is no need for a graduated RTW plan [190] until the individual is no longer experiencing suicidal ideation and the anxiety disorder has been stabilized.

Initially, the individual may report severe anxiety symptoms, but with careful probing, the day-to-day variability in these symptoms is obtained. This is an important factor to keep in mind regarding work capacity.

Mild or moderate anxiety does not usually require workplace accommodations or absence. Instead, the individual's workplace performance may decrease (e.g., presenteeism). If this is observed and the individual's performance has been generally productive in the past, it is important to have the individual evaluated.

Keeping this in mind, it is important to understand that most patients with anxiety disorders do not require any work restrictions or accommodations. Even with reported severe anxiety, any workplace leave or accommodations should be temporary and only occur if severe impairment is objectively determined, significant cognitive impairment exists, and/or the individual has suicidal ideation [190]. However, the majority of individuals with anxiety disorders who receive appropriate treatment recover [191-193].

All types of anxiety disorders are responsive to specific types of psychological treatment. Specifically, work-focused CBT is associated with the best RTW outcomes. Work-focused CBT helps individuals with anxiety disorders return to work sooner and treatment costs are significantly less than other types of psychological treatment [194-198].

The most common workplace limitations or accommodations that are sometimes needed for patients with anxiety disorders involve the use of benzodiazepines, which should consequently be avoided. Besides being highly addictive, extensive literature supports considerable impairments associated with benzodiazepine use including memory [199, 200], cognition (e.g.,

visuospatial ability, speed of processing, and verbal learning) [201], sedation [201], risk of motor vehicle collisions [202, 203], dementia [203, 204], and falls [205, 206]. Thus, numerous other treatments are indicated before consideration of a benzodiazepine trial. Benzodiazepines are ill-advised for primary or secondary treatment of patients with anxiety disorders, especially for those performing safety-sensitive/safety-critical work or cognitively intensive work (see the [Benzodiazepines recommendations](#)).

Perceived Cognitive Impairment versus Negative Thinking

The self-report of social and cognitive impairment in functioning are frequently mentioned by individuals with anxiety disorders as well as treating professionals [196, 197, 207, 208].

However, when reviewing the empirical research regarding the assessment of cognitive impairment, it is not typically confirmed with standardized psychological testing. This lack of support for social and cognitive impairment is based on the review of the current empirical research [209].

Frequently, individuals with psychological conditions report perceived cognitive impairment. In completing an extensive literature review, some studies claimed to have examined cognitive impairment in functioning in individuals with anxiety disorders. However, many studies were specific to obsessive compulsive disorder (OCD), which is no longer classified as an anxiety disorder in the DSM-5. In addition, purported associations between anxiety disorders and cognitive functioning problems are weakened by important factors, including utilization of only one measure related to cognitive functioning, a lack of randomization, poorly matched subjects (e.g., a greater number of males vs. females), small sample size, reliance on screening tools, omission of standardized psychological tests to identify reported cognitive problems, and lack of homogeneity among the people studied [134, 135]. A minimum of two standardized psychological tests that are specific to anxiety disorders must be utilized because this increases the likelihood that the individual is experiencing these concerns across measurements [210-216].

Moreover, any cognitive impairment reports by an individual with anxiety disorder require the usage of full scales of each standardized psychological test that is administered (e.g., all subtests within each test). The reason is that cognitive functioning is comprised of multiple functions, not one. Thus, an empirical study that reports a significant finding of cognitive impairment but utilizes only one subtest has not demonstrated widespread cognitive impairment. Frequently, individuals may have lower scores in some subtests, but when the overall testing results are examined, the person's cognitive functioning is still within the "normal" range (e.g., within the middle of the distribution where 68.26% of the population scores. In other words, 68% of scores for a normal bell curve will lie between -1 and +1 standard deviation). When a test score falls within this range, this demonstrates functioning that is considered "normal" or "average" functioning. In this instance, if a person's test scores fall within this range, the individual's cognitive functioning is not considered impaired.

Although a single systematic review of 40 studies found that individuals with GAD have worse performance on selective attention, working memory, cognitive inhibition, and decision making, this was related only to stimuli that individuals perceived as threatening or anxiety-producing. Another study found that individuals with GAD may exhibit poor inhibition in memory, decreases in working memory, and inductive reasoning. However, processing speed, verbal working memory, verbal fluency, and episodic memory did not predict future GAD of experiencing future episodes; it was acknowledged that additional research needed to be completed before any of these potential concerns can be confirmed as occurring routinely with GAD [134-137, 217].

Consequently, those with an anxiety disorder who report substantial social and cognitive functioning impairment must be assessed with a comprehensive evaluation and thorough psychological testing to confirm or rule out any potential cognitive impairment [134, 135, 217]. The results of this testing must be reviewed with the individual so that the individuals' concerns are acknowledged and normalized.

Moreover, workplace psychosocial issues must be identified as part of the assessment and treatment process for individuals with anxiety disorders. Typically, the individual's perception of workplace situations versus organizational policy plays a role in promoting psychosocial issues. However, psychosocial issues are not psychological conditions. They have no diagnostic criteria. Instead, psychosocial issues may impede treatment progress and outcomes [113, 165-174, 209, 218].

In addition, when an individual becomes physically sedentary, this contributes to ill mental health. Instead, it is essential for individuals with anxiety disorders to stay active and to participate in regular exercise as a means for managing physical symptoms of anxiety (see [Exercise guidance](#)) [219-224].

Safety Considerations

Many jobs do not have a high degree of safety issues. Likewise, the severity of most anxiety disorders does not result in substantial reduced capacity to work. Instead, the individual feels uncomfortable in the workplace, but can still complete workplace duties. In those instances, it is important to focus on a SAW plan with the individual and employer. It is important to note that an SAW plan does not require the individual to take time off for psychological treatment. Instead, the individual continues to go to work and receive psychological treatment (e.g., CBT) concurrently. However, benzodiazepines are problematic for both safety-critical work and cognitively demanding work (see above).

When an individual is reporting severe anxiety symptoms, the evaluation must focus on the individual's capacity to work as well as the safety-sensitivity issues associated with some types of jobs (e.g., medical professionals, commercial airline captains, commercial truck drivers). In those jobs with a high need for safety of self and others as well as the capacity to make well-reasoned decisions, it is essential to thoroughly evaluate employer reports of safety concerns,

workplace accidents, and the individual's self-reported concerns regarding cognitive and physical functioning. This type of assessment is likely to require the individual's job description as well as speaking directly with the employer regarding the individual's past and present workplace performance. Communication with the individual's employer can only take place after a release has been signed by the individual [117, 118].

Stay-at-Work Plans

Professional management and treatment to facilitate the individual staying in the workplace must identify workplace stressors, as well as how the individual copes with these stressors [225].

For individuals with adjustment disorder with anxious mood, panic disorder, and generalized anxiety disorder, the primary focus in any treatment is to facilitate the individual staying at work. Ruminative thinking plays a primary role in individuals' perceptions regarding capacity and work. Individual perceptions of workplace stress and the ability to cope with the stress play a large role in the individual modulation of job stressors. Individuals with positive perceptions of their ability to cope with workplace stressors tend to have a high degree of resiliency. Individuals who view the workplace negatively may be less resilient to workplace stressors, such as increased job demands, frequent interruptions, and perceived lack of job support. Nonoccupational factors that are associated with individual perception of capacity to work include family stressors and financial issues [102, 109, 113, 117, 118, 122, 175, 176, 226].

Cognitive behavioral therapy that focuses specifically on the workplace (w-CBT) teaches new strategies to cope with workplace demands and increases productive problem-solving. These CBT strategies are generally associated with improvements in workplace perceptions as well as providing new skills to address issues as they arise in the workplace (see [CBT recommendations](#)). w-CBT is typically provided while the individual remains working and is time-limited [122-128, 134, 163, 164, 194, 227-237].

In addition, more recent advancements in the psychological treatment of anxiety disorders involve ascertaining the individual's level of cognitive flexibility versus rigid thinking. In addition to CBT, the use of exposure to triggers for an individual's anxiety is also quite helpful in rapidly reducing the individual's perception of being unable to function as well as addressing habituation within the limbic system with repeated exposures [238-242].

Return-to-Work Plans

The primary occupational factors associated with common anxiety disorders and workplace absence include the diagnosis of an anxiety disorder, the individual's perceptions of RTW barriers, and the same factors associated with adjustment disorder with anxious mood and panic disorder. The primary nonoccupational factors associated with workplace absence and generalized anxiety disorder are the same those that occur for adjustment disorder with anxious mood and panic disorder [183, 218-220, 227, 229, 231, 233, 243-267].

However, anxiety disorders frequently occur with many other psychological and physical conditions. The presence of a co-morbid condition may impact the severity of anxiety that is reported as well as a perceived reduction in work capacity. Consequently, it is essential to include an evaluation of comorbid conditions when assessing potential workplace impairment in functioning [268, 269].

As noted earlier, the severity of an anxiety disorder is not frequently considered regarding workplace absence. Instead, the diagnosis of anxiety disorder itself is often the reason for workplace absence. As Table 1 demonstrates, there is a continuum of anxiety conditions that range from mild/moderate to more significant anxiety. Typically, anxiety conditions that produce mild to moderate anxiety, such as adjustment disorder with anxious mood and panic disorder, do not result in substantial functional impairments. Generalized anxiety disorder may cause significant anxiety symptoms that are temporarily disruptive to everyday life. However, even in those instances, the ability to function is generally not impaired. Instead, the individual's focus on anxiety-based thoughts may be disruptive because he or she remains highly focused on the fearful thoughts in an effort to control and reduce the anxiety itself. Therefore, the diagnosis of anxiety disorder alone is not sufficient as a rationale for placing an individual on workplace leave. Moreover, if the individual has a history of recurrent anxiety episodes, it is important to keep in mind that a prior anxiety remission and RTW goals typically lead to the same treatment goal for the current anxiety episode [253, 270-285].

For individuals with anxiety disorders who are on work leave, the primary goal is to address the individual's return to work. As noted previously, for individuals with adjustment disorder with anxious mood or panic disorder, there is usually no need for the individual to take a leave of absence. In the instance where the individuals with these disorders has been on leave, the goal is to facilitate return to work. There is typically no need for a graduated return to work as discussed above and the individual can return to work to work immediately. This is also true for generalized anxiety disorder [286, 287].

Regarding the diagnosis of anxiety disorders, it is imperative to evaluate the severity of anxiety disorder. This type of assessment cannot be based on subjective opinion or perception. Frequently, those with an anxiety disorder do not experience any sustained impairment in functioning. Instead, the periods in which the individual experiences anxiety are typically short, discrete episodes versus constant anxiety. Impairment is usually temporary until medication is fully titrated, sufficient time has passed for medication efficacy, and psychotherapy (e.g., CBT) has been provided. Most individuals with severe anxiety disorders and no suicidal ideation do not require hospitalization. They are also unlikely to be a risk to themselves or others [288-298].

For those who report severe anxiety and reduced capacity to work that has been confirmed through psychological testing, intensive outpatient psychotherapy (IOP) is important to help regain functioning as soon as possible. Typically, IOP treatment provides CBT, acceptance and commitment therapy (ACT), or interpersonal psychotherapy (IPT) treatment to address the

individual's ruminative thinking. This type of thinking is called *cognitive triad*. The cognitive triad consists of negative views about the world, oneself, and the future [162, 299]. Although individuals with depressive disorders are found to experience the cognitive triad, this also occurs with anxiety disorders. Again, w-CBT typically is most effective for addressing the misperceptions regarding capacity to work as well as the cognitive triad that may occur with anxiety disorders [194-197, 233].

As part of w-CBT treatment, the individual is then taught problem-solving skills to address issues that the individual perceives as overwhelming. Usually, IOP treatment is coordinated with psychiatric treatment so that the individual's medication is prescribed by a psychiatrist. Psychiatric involvement is essential so that the individual's medication can be prescribed and titrated to a therapeutic dose [288, 300-305].

Specific to individuals with anxiety disorders, a gradual workplace exposure to the events and situations that trigger anxiety plays a critical role in helping the person to reduce the sense of becoming overwhelmed. This also allows the individual to practice the techniques learned in w-CBT to enhance the individual's success in the RTW process [165, 306-308].

Individuals who report severe anxiety symptoms with suicidal ideation may be at risk of harming themselves [309]. When this occurs and the person has suicidal intent and plan, psychiatric hospitalization is usually required to provide intensive treatment and to stabilize the individual [309-311]. Also, anxiety typically is not constant, as it comes and goes for periods of time (e.g., minutes versus an entire day).

Even after the individual is released from the psychiatric hospital, psychological and psychiatric treatment continues. It is essential that medications are given at a therapeutic dose because the continuation of symptoms is a primary reason that laypeople and professionals alike believe that anxiety disorders are permanent conditions. All types of anxiety conditions may be brought under control and the individual can regain previous level of functioning in life [260, 312-322].

When recovery is established, it is time to start the RTW process [261, 320, 323-331]. If the person has been hospitalized or off work for 3 months or longer, the graduated RTW process outlined in the [Workplace Mental Health Introduction](#) can occur. Usually, this process requires coordination with the workplace [332-345]. Reaching out to an employer's human resource department is an effective way to start the process. The graduated RTW process is discussed so that all parties are aware that it is time limited. Typically, long-term workplace accommodations are not necessary [346, 347].

An SAW goal is an important part of any treatment process with individuals who have a mental health condition, as it helps maintain or increase function. Many individuals with diagnosed mental disorders continue to work each day. As discussed earlier, symptoms are frequently confused with impairment in functioning. In addition, the diagnosis of a mental health condition is often noted as the reason for purported impairment in functioning. However, as with many other mental health disorders, the majority of those with anxiety disorders

experience mild to moderate impairment in functioning. With w-CBT, individuals can learn more adaptive behaviors to manage workplace situations. Table 1 provides SAW recommendations to consider regarding the more common anxiety disorders.

Adjustment disorder with anxious mood is a temporary emotional response to a situation or an event, such as a death or divorce. The majority with this disorder will experience no impairment in functioning to mild impairment related to some mood disturbance, coupled with sleep disruption. Most individuals with this condition experience lesser anxiety symptoms for several weeks to a few months. In most cases, the adjustment disorder with anxious mood resolves.

For those who are diagnosed with panic disorder, it is important to note that the individual may experience a panic attack with physical symptoms of sympathetic arousal, such as increased heart rate, increased rate of respiration, and increased muscular tensing. Most panic attacks last 15–20 minutes and then resolve. However, the individual learns to fear the panic attacks and is concerned regarding public embarrassment or a potential health concern, such as a heart attack. Gradually, the person may become conditioned to fear potential future panic attacks. Much of an individual's thinking focuses on how to avoid events and situations where a person may feel trapped, such as in a work meeting. The individual may experience regular thoughts regarding future panic attacks. However, once the panic attack is resolved, there is no sustained impairment in functioning that continues to exist with panic disorder.

With generalized anxiety disorder (GAD), the individual has not necessarily experienced a stressful event or situation that the person is trying to avoid. Instead, GAD-related anxiety is related to no specific identified situations. It is an individual's generalized response to stressful events that occur in everyday life. Individuals with controlled GAD (usually those who are receiving treatment or have completed treatment) may experience a mild to moderate recurrence of anxiety-based thoughts. However, the individual's ability to function in most life activities remains intact. In cases where no diagnosis has been made and/or the individual has not begun treatment, the person may experience more significant anxiety-based thoughts. With appropriate treatment, the individual's level of functioning improves as more adaptive strategies are learned to manage workplace stressors as they arise.

Table 1. Stay-at-Work (SAW) Issues and Recommendations for the Most Common Workplace Anxiety Disorders*

	Adjustment disorder with anxious mood	Panic disorder	Generalized anxiety disorder	Phobic responses
Level of impairment in functioning	None to mild	None to moderate impairment; panic attacks usually last 15-20 minutes, with the physical arousal symptoms resolving.	Mild to severe	Varies; a graduated exposure approach to the workplace facilitates both SAW and RTW processes, as the individual learns to manage and reduce anxiety related to the workplace.
Assessment of potential psychosocial issues	Yes	Yes	Yes	Yes
Permanent work restrictions and accommodations	No; however, the individual may require a temporary leave from work (e.g., 1-2 weeks) for a death or other serious life-altering event.	No; however, the employer may improve the individual's ability to SAW by allowing periodic breaks to manage a panic attack when it occurs.	No for nearly all cases; however, the employer may improve the individual's ability to SAW by allowing periodic breaks to manage anxiety-based thoughts. Need to formally assess potential / reported cognitive impairment and workplace safety issues.	No; the primary goal is to reduce the individual's avoidance of situations or events where they experience anxiety in the workplace.

*Assumes the guidance regarding avoidance of impairing medications has been followed and there are not safety-sensitive work issues.

The RTW process has been discussed in the [Workplace Mental Health Introduction](#) and other modules such as [Depressive Disorders](#). Table 2 provides general recommendations to consider when an individual has been out of the workplace related to one of the common anxiety disorders. If the workplace absence is less than 3 months, no graduated RTW plan is generally

needed. If the workplace absence is 3 months or longer, then a graduated RTW plan (discussed in the [Workplace Mental Health Introduction](#)) may be necessary.

Any time that an individual is absent from the workplace, evidence-based treatments are provided and the setting of a RTW goal should occur. Usually, mental health treatment can continue as part of the individual's RTW process. It is common for an individual who has been absent from the workplace for a lengthy period to experience anticipatory anxiety regarding returning to work. It is important to not confuse this temporary anticipatory anxiety with a continuation of an anxiety disorder. Instead, this type of anxiety can be discussed as part of the treatment process to normalize it.

Most individuals who have been off work for a lengthy period will be fully engaged in the treatment process. After a person has been engaged in an effective, evidence-based treatment process for several weeks to months, the anxiety condition should be greatly reduced. Thus, impairment in functioning is likely to improve considerably.

Table 2. Return-to-Work Recommendations for the Most Common Workplace Anxiety Disorders*

	Adjustment disorder with anxious mood	Panic disorder	Generalized anxiety disorder	Phobic responses
Level of Impairment in functioning	None to mild	None to mild; thoughts may occur periodically that are focused on avoiding events and situations where panic attacks occurred.	Mild to moderate; individuals with controlled GAD may experience a mild to moderate recurrence of anxiety-based thoughts. Severe†; individuals with severe GAD may experience significant recurrence of anxiety-based thoughts.	Varies; a graduated exposure approach to the workplace facilitates both SAW and RTW processes, as the individual learns to manage and reduce anxiety related to the workplace.
Assessment of potential psychosocial issues	Yes	Yes	Yes	Yes
Permanent work restrictions and accommodations‡	No	No; however, the employer may help improve the	No; however, the employer may help improve the	No

		individual's SAW by allowing periodic breaks to manage a panic attack if it occurs in the workplace.	individual's SAW by allowing periodic breaks to manage anxiety-based thoughts. Need to formally evaluate and assess potential / reported sustained cognitive impairment and workplace safety issues.	
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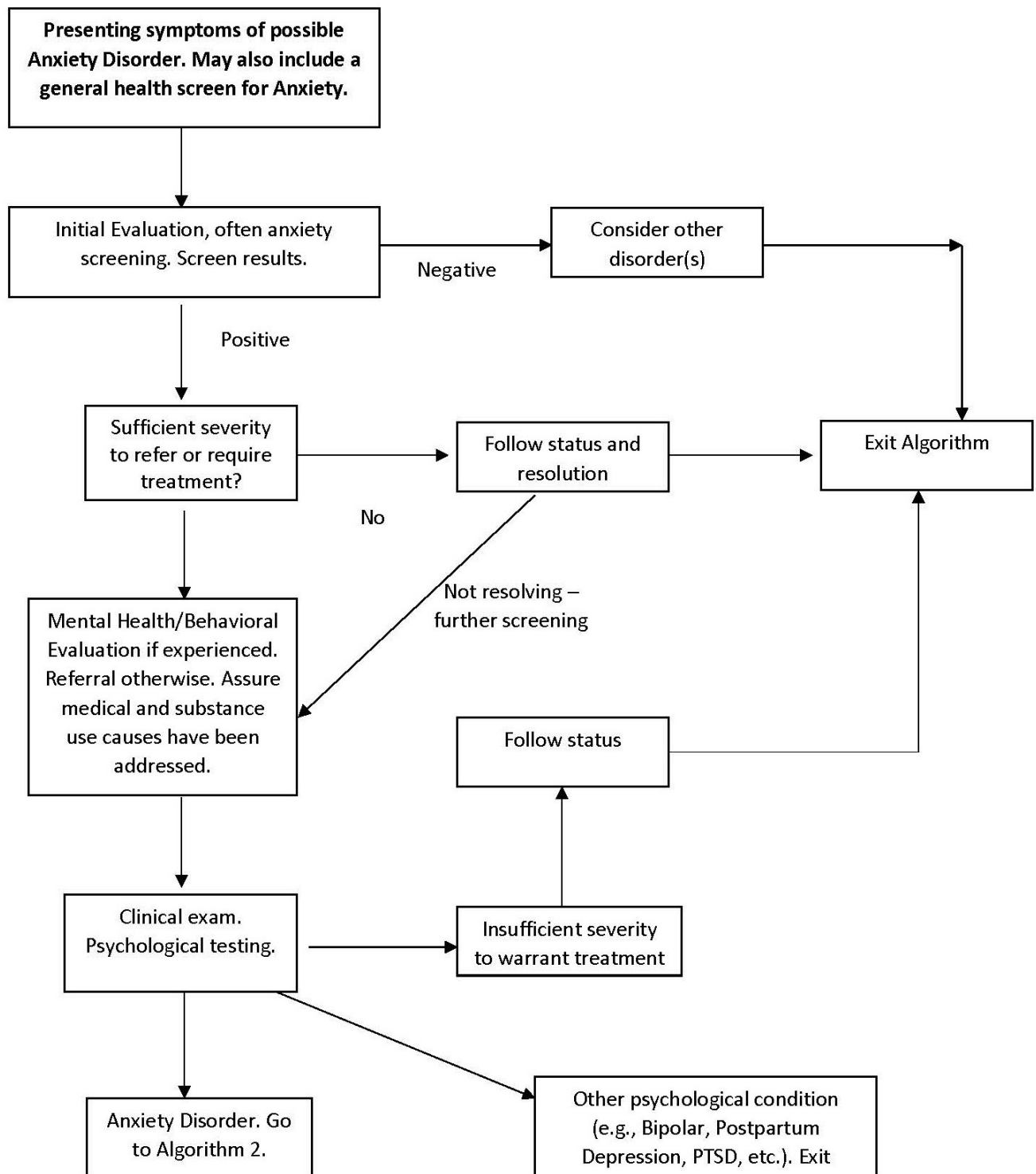
* After a >3-month workplace absence during which the individual has been receiving appropriate treatment; assumes the guidance regarding avoidance of impairing medications has been followed and there are not safety-sensitive work issues.

† A person should already have received effective, evidence-based treatment and be stable. Thus, it should be quite rare that someone would continue to have severe symptoms at 3 months. RTW/SAW is nearly always successful. Greater intensity of treatment, interaction with the employer, and plans to address the anxiety when it occurs all improve SAW/RTW if and when absences are required.

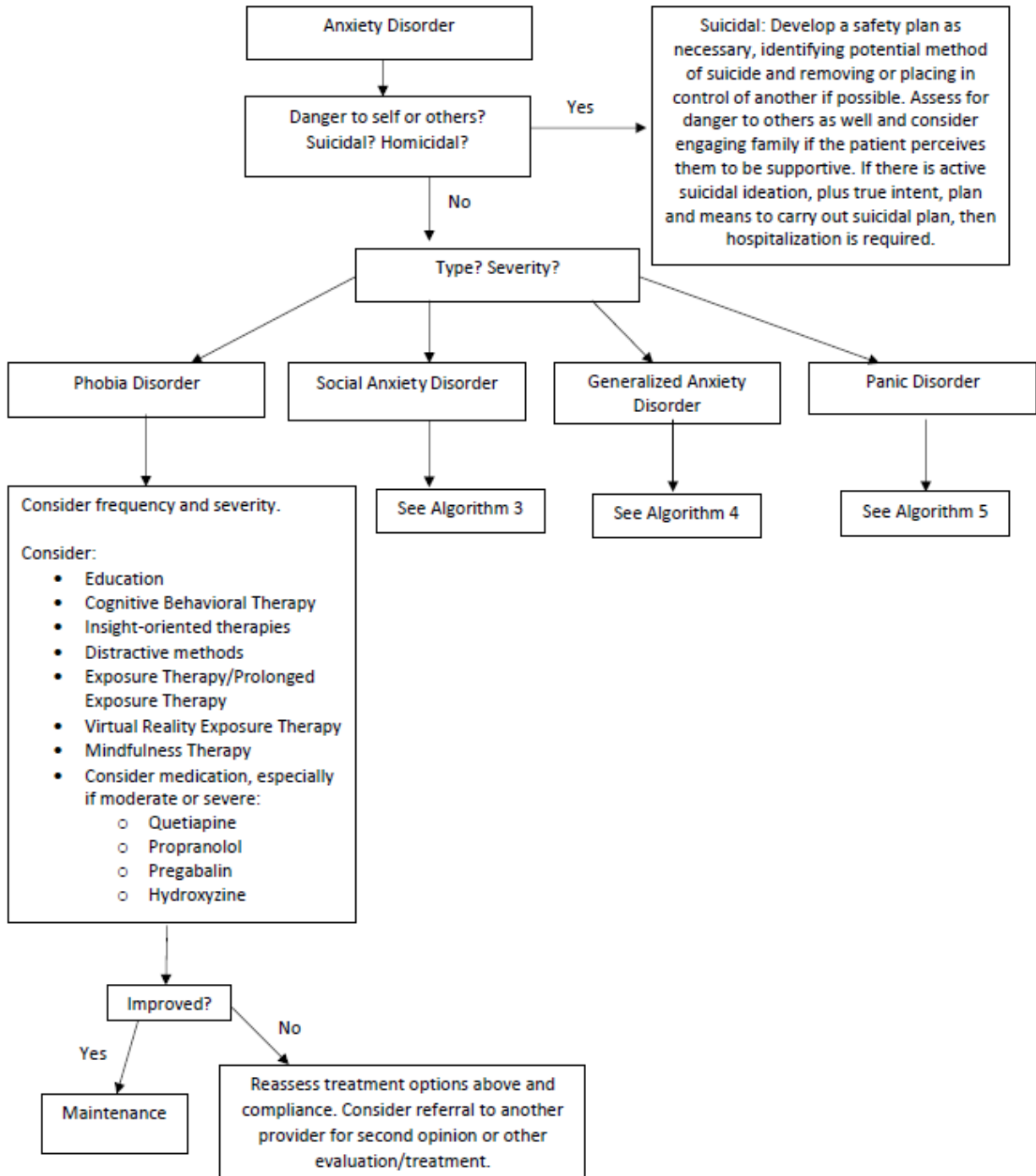
‡ After >3 months of absence during which the individual has been receiving treatment.

Algorithms

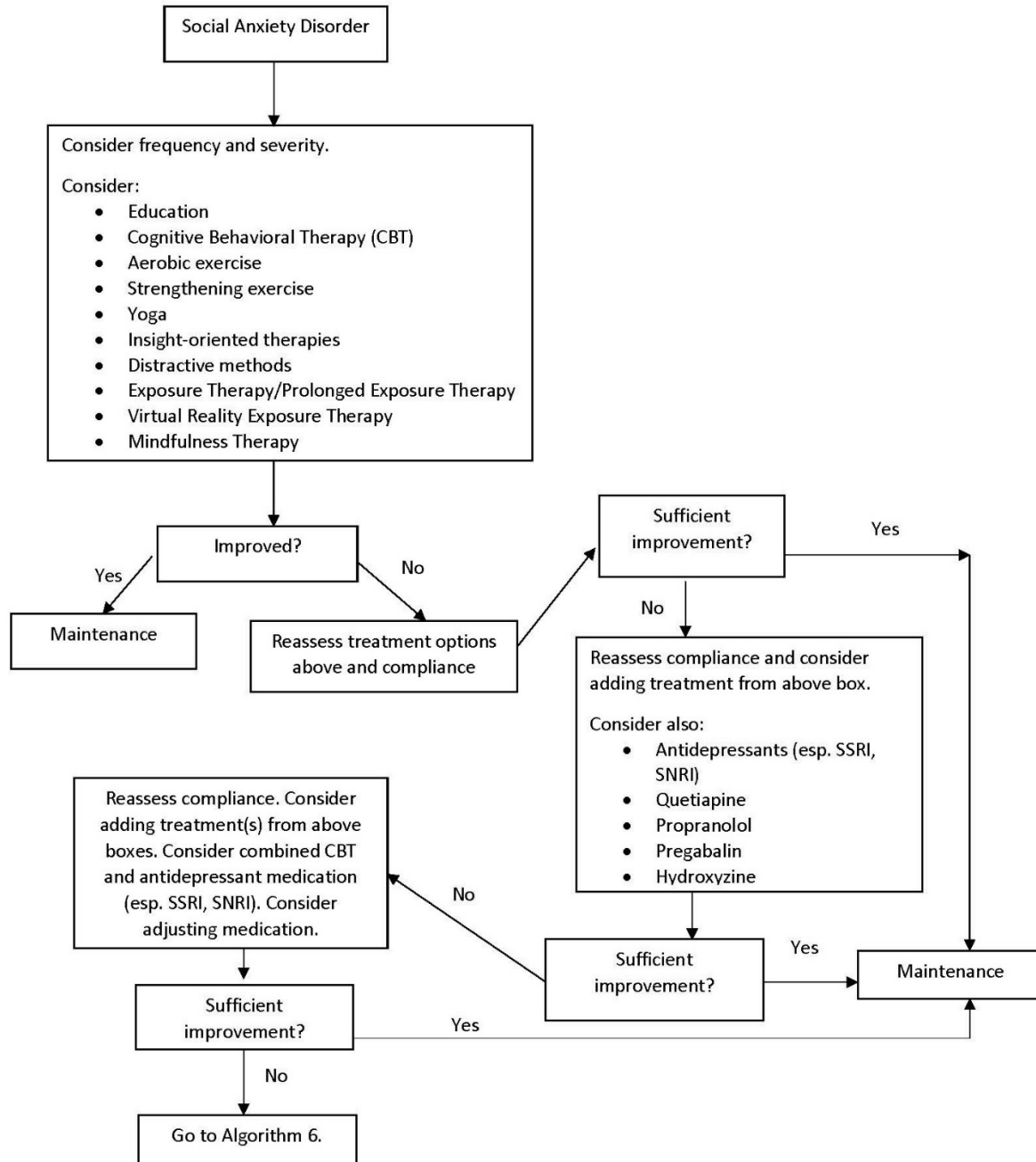
Algorithm 1. Presenting Symptoms of Possible Anxiety Disorder



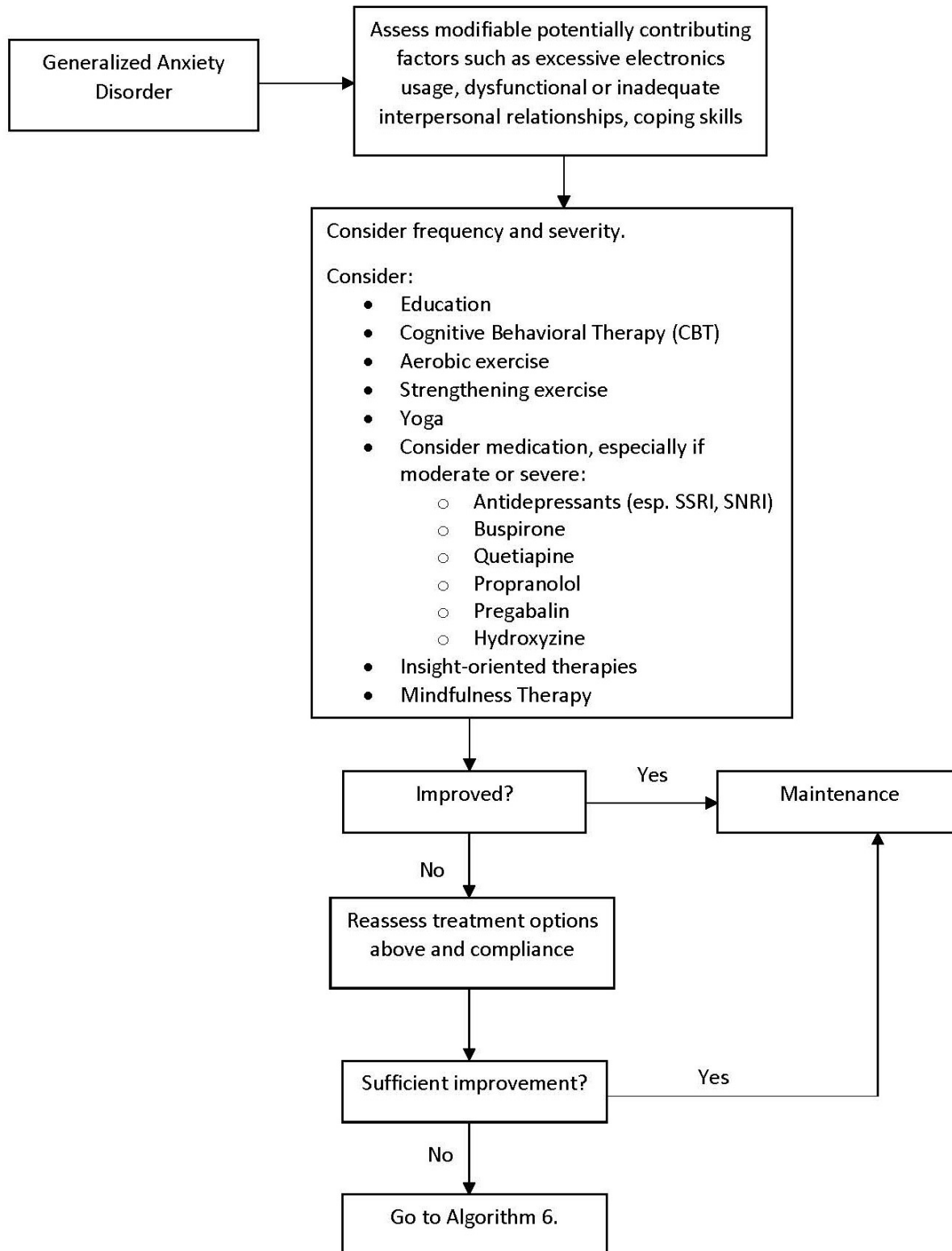
Algorithm 2. Management of Anxiety Disorder by Type



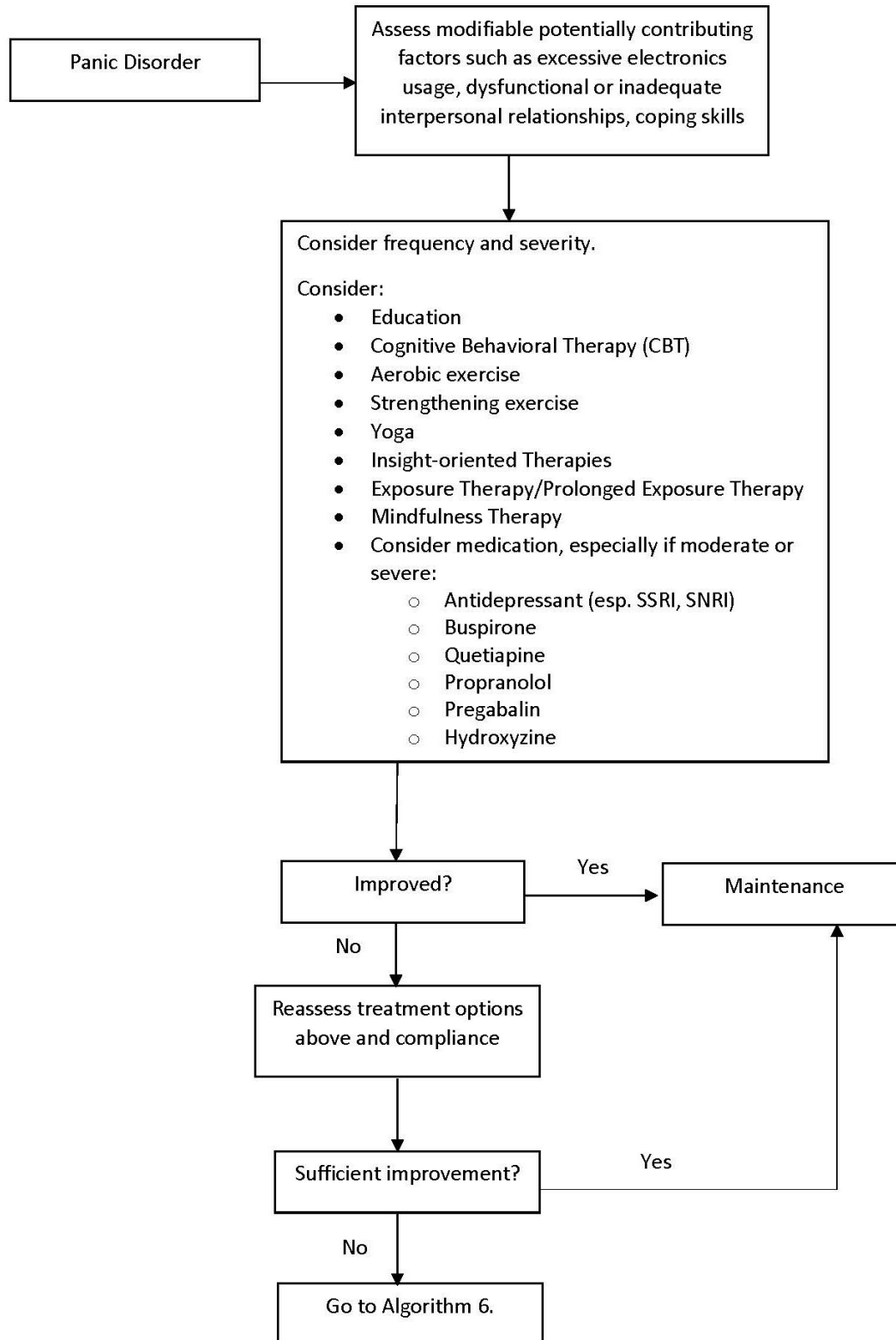
Algorithm 3. Management of Social Anxiety Disorder



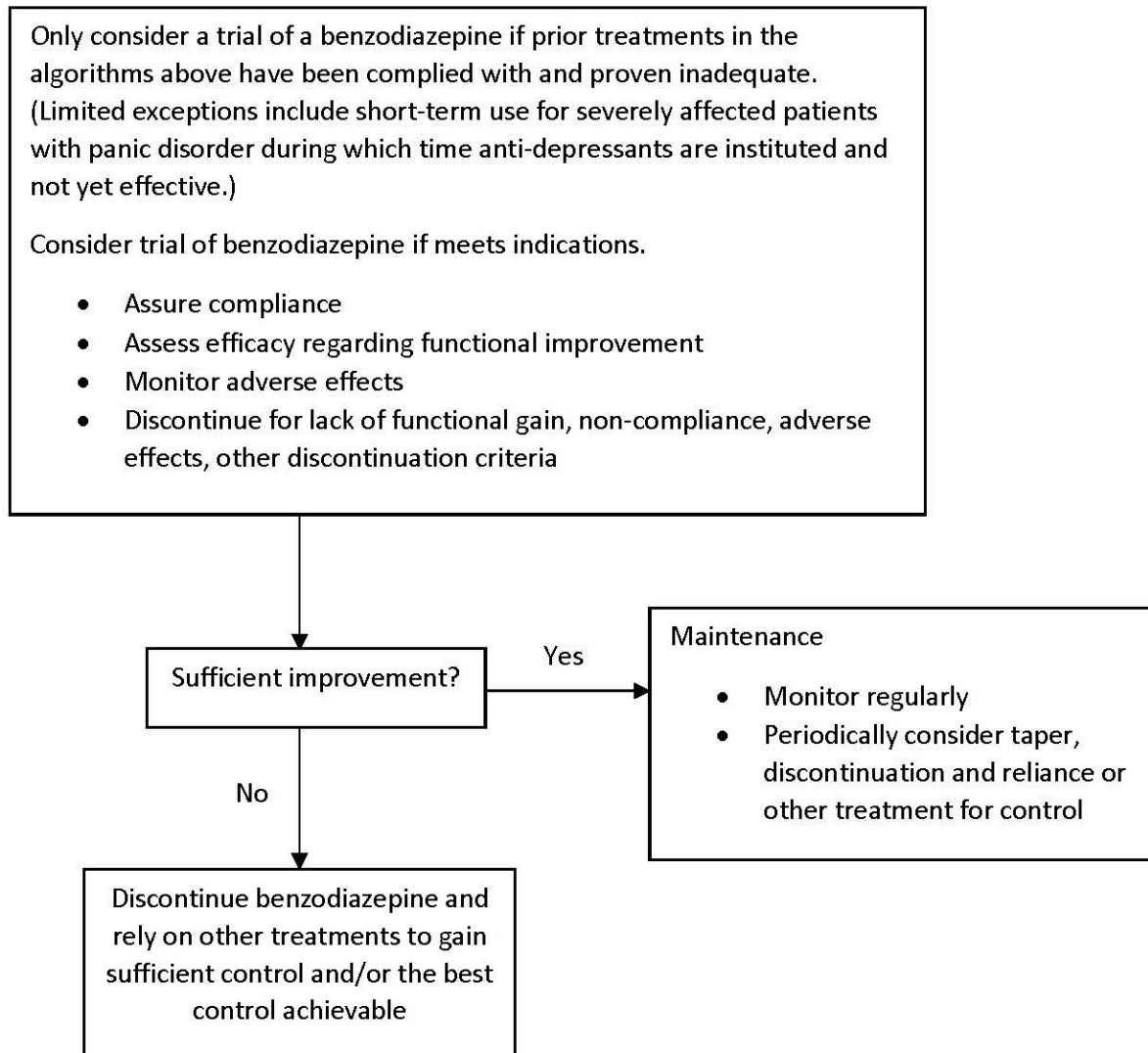
Algorithm 4. Management of Generalized Anxiety Disorder



Algorithm 5. Management of Panic Disorder



Algorithm 6. Benzodiazepine Trials



Treatment Overview

When analyzing the treatment of anxiety disorders, it is important to note that there are some variations, including by the type of anxiety disorder.

Prevention

There are no quality data for primary prevention of anxiety. Considering that evidence suggests aerobic exercise is an effective treatment for anxiety disorders, it may be reasonable to infer that aerobic exercise would have a significant role in primary and secondary prevention.

Suicidality

Suicidality is considerably more common among those with depressive disorders than anxiety disorders. Nevertheless, assessment and treatment of suicidality important in the treatment of individuals with anxiety disorders (see [ACOEM Depressive Disorders Guideline](#)).

Psychological Management

Evidence consistently supports CBT for the treatment of anxiety disorders. There are several types of CBT with evidence of efficacy, including computer-assisted CBT, bibliotherapy, and acceptance and commitment cognitive behavioral therapy. There is evidence suggesting a combined approach of CBT with antidepressants is effective for treatment of anxiety disorders. In addition, there is evidence that CBT is effective in reducing future relapses. Modifiable contributory factors (e.g., excessive electronics usage, dysfunctional or inadequate interpersonal relationships, coping skills) should also be addressed. Exposure therapy, prolonged exposure therapy, and virtual reality exposure therapy are effective for the treatment of phobias and social anxiety disorder. Distractive methods are also effective for social anxiety disorder.

Pharmacological Management

Management of anxiety disorders should include a review of mood-altering medications that may be contributing factors, such as opioids and cannabinoids. Pharmaceutical treatment of anxiety disorders with multiple classes of antidepressants and other medications has consistent evidence of efficacy. Selection of a particular antidepressant or other medication is often based on a desire to treat accompanying symptoms, such as insomnia, and/or to avoid particular adverse effects. Other medications with quality evidence of efficacy include quetiapine, pregabalin, propranolol, and hydroxyzine. Although benzodiazepines have been widely used for treatment of anxiety disorders, they are highly addictive and have major adverse effects that include withdrawal symptoms. Thus, benzodiazepines may be indicated, but only after other options have been utilized, complied with, and there is clear documentation of functional gain during a trial of medication. If treatment of insomnia beyond CBT and antidepressants is needed, selection of a nonbenzodiazepine medication is advisable (e.g., agomelatine, eszopiclone, nefazodone, zolpidem).

Risk and Causation

See the [ACOEM Workplace Mental Health Guideline Introduction](#).

Symptoms and Signs

Generalized Anxiety Disorder

Generalized anxiety disorder has many symptoms and signs. Although all individuals are likely to experience some anxiety at various times, individuals with anxiety disorders have symptoms that are often excessive or incapacitating for the given situation. Common symptoms include the following:

- Excessive worrying and tension
- Impractical idea of problems
- Irritation
- Consistently feeling restlessness
- Difficulty concentrating
- Startled easily
- Constantly needing to use the restroom
- Intrusive thoughts
- Inability to tolerate uncertainty
- Avoiding situations

Common physical symptoms and signs that a person with generalized anxiety disorder may experience also include the following:

- Muscle stiffness
- Headaches
- Feeling nauseous
- Shaking or trembling
- Trouble with sleep, including falling asleep and frequent arousals

Social Anxiety Disorder

Social anxiety disorder is characterized by the fear of everyday social interactions. Symptoms and signs of social anxiety disorder can include the following:

- Anxiety in anticipation of a feared activity or event
- Intense fear or anxiety in a social situation
- Fear of situations with judgment
- Worrying about embarrassment or humiliation
- Intense fear of interacting or talking with strangers
- Avoidance

Physical symptoms and signs include the following:

- Nausea
- Shortness of breath or difficulty of breathing
- A choking sensation
- Hot flushes or chills

- Dry mouth
- Headaches
- Dizziness
- Tightness or pain in the chest
- Tachycardia
- Ringing in the ears
- Confusion or disorientation

Phobic Disorders

People exhibiting phobic disorders will typically have fears in one or more of the following categories, including the following:

- Stressful situations
- Enclosed spaces
- Animals or insects
- Nature
- Accidents with medical procedures
- Loud noises

Symptoms and signs of a phobic disorder include the following:

- Nausea
- Shortness of breath or difficulty of breathing
- Choking sensations
- Hot flashes or chills
- Dry mouth
- Headaches
- Dizziness
- Tightness or pain in the chest
- Tachycardia
- Ringing in the ears
- Confusion or disorientation

Panic Disorders

Panic attacks are sudden episodes of intense fear that trigger severe physical reaction without any real danger or cause. Panic disorders occur when panic attacks manifest at a high rate, which impair daily activities. Symptoms and signs are typically relatively sudden in onset and include the following:

- Nausea
- Shortness of breath or difficulty of breathing
- Choking sensations
- Hot flashes or chills
- Dry mouth

- Headaches
- Dizziness
- Tightness or pain in the chest
- Tachycardia
- Ringing in the ears
- Confusion or disorientation

Agoraphobia

Agoraphobia is an anxiety to phobic disorders and is the fear of being trapped in certain places or situations, which can leave a person panicked, feeling helpless, or embarrassed. Physical reactions and symptoms are similar to those of phobic disorders. A person with agoraphobia may fear the following:

- Leaving home alone
- Crowds or waiting in line
- Enclosed spaces
- Open spaces (e.g., parking lots, restaurants, public mall)
- Public transportation

Substance or Medication-Induced Anxiety Disorder

Substance or medication-induced anxiety disorder is typically diagnosed as anxiety or panic attacks directly related to or caused by a consumed or used substance or medication. Temporality is a key feature of this disorder; thus, the symptoms must be exhibited shortly after taking or withdrawing from the substance or medication. Symptoms and signs are closely related to those of generalized anxiety disorder and phobic disorders as these are typically the same types of sensations a person is experiencing.

A few of the common substances that have been linked to substance or medication-induced anxiety disorder include the following:

- Alcohol
- Caffeine
- Cannabis
- Sedatives
- Phencyclidine

History and Psychological/Psychiatric Examination

See the [ACOEM Workplace Mental Health Guideline Introduction](#).

Medical History Questionnaire

See the [ACOEM Workplace Mental Health Guideline Introduction](#).

Diagnosis

Medical and pharmaceutical causes of anxiety disorders should be ruled-out and/or addressed (e.g., hyperthyroidism, other endocrine disorders, cardiac disorders, dysrhythmias, pulmonary disorders, stimulant use, marijuana).

Diagnostic Criteria

There are different diagnostic categories of anxiety disorders and the diagnostic criteria differ by the classification system.

DSM-5 criteria anxiety disorders include: Separation anxiety disorder, selective mutism, specific phobia, social anxiety disorder (social phobia), panic disorder, panic attack specifier, agoraphobia, generalized anxiety disorder, substance/medication-induced anxiety disorder, anxiety disorder due to another medical condition, other specified anxiety disorder and unspecified anxiety disorder.

ICD-10 categories of anxiety disorders include: Phobic anxiety disorders, agoraphobia, social phobias, specific (isolated) phobias, other phobic anxiety disorders, phobic anxiety disorder (unspecified), other anxiety disorders, panic disorder (episodic paroxysmal anxiety), generalized anxiety disorder, mixed anxiety and depressive disorder, other mixed anxiety disorders, other specified anxiety disorders, and anxiety disorder (unspecified).

A complete listing of the diagnostic categories and criteria in use in the DSM-5 is available [348]. The ICD-10 criteria are also available and are more commonly utilized outside of the United States [349]. Succinct descriptions of some of the common DSM-5 anxiety disorders are then followed by ICD-10 descriptions.

DSM-5 Criteria

Generalized Anxiety Disorder

“A. Excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least 6 months, about a number of events or activities (such as work or school performance).

B. The individual finds it difficult to control the worry.

C. The anxiety and worry are associated with three (or more) of the following six symptoms (with at least some symptoms having been present for more days than not for the past 6 months):

Note: Only one item is required in children.

1. Restlessness or feeling keyed up or on edge.
2. Being easily fatigued.
3. Difficulty concentrating or mind going blank.

4. Irritability.
5. Muscle tension.
6. Sleep disturbance (difficulty falling or staying asleep, or restless, unsatisfying sleep).

D. The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

E. The disturbance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition (e.g., hyperthyroidism).

F. The disturbance is not better explained by another mental disorder (e.g., anxiety or worry about having Panic Attacks in Panic Disorder, negative evaluation in Social Anxiety Disorder [Social Phobia], contamination or other obsessions in Obsessive-Compulsive Disorder, separation from attachment figures in Separation Anxiety Disorder, reminders of traumatic events in Post-Traumatic Stress Disorder, gaining weight in Anorexia Nervosa, physical complaints in Somatic Symptom Disorder, perceived appearance flaws in Body Dysmorphic Disorder, having a serious illness in Illness Anxiety Disorder, or the content of delusional beliefs in Schizophrenia or Delusional Disorder)."

Social Anxiety Disorder (Social Phobia)

"A. Marked fear or anxiety about one or more social situations in which the individual is exposed to possible scrutiny by others. Examples include social interactions (e.g., having a conversation, meeting unfamiliar people), being observed (e.g., eating or drinking), and performing in front of others (e.g., giving a speech).

Note: In children, the anxiety must occur in peer settings and not just during interactions with adults.

B. The individual fears that he or she will act in a way or show anxiety symptoms that will be negatively evaluated (i.e., will be humiliating or embarrassing: will lead to rejection or offend others).

C. The social situations almost always provoke fear or anxiety.

Note: In children, the fear or anxiety may be expressed by crying, tantrums, freezing, clinging, shrinking, or failing to speak in social situations.

D. The social situations are avoided or endured with intense fear or anxiety.

E. The fear or anxiety is out of proportion to the actual threat posed by the social situation and to the sociocultural context.

F. The fear, anxiety, or avoidance is persistent, typically lasting for 6 months or more.

G. The fear, anxiety, or avoidance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

H. The fear, anxiety, or avoidance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition.

I. The fear, anxiety, or avoidance is not better explained by the symptoms of another mental disorder, such as Panic Disorder, Body Dysmorphic Disorder, or Autism Spectrum Disorder.

J. If another medical condition (e.g., Parkinson's disease, obesity, disfigurement from burns or injury) is present, the fear, anxiety, or avoidance is clearly unrelated or is excessive."

Panic Disorder

"A. Recurrent unexpected panic attacks. A panic attack is an abrupt surge of intense fear or intense discomfort that reaches a peak within minutes, and during which time four (or more) of the following symptoms occur:

Note: The abrupt surge can occur from a calm state or an anxious state.

1. Palpitations, pounding heart, or accelerated heart rate.
2. Sweating.
3. Trembling or shaking.
4. Sensations of shortness of breath or smothering.
5. Feelings of choking.
6. Chest pain or discomfort.
7. Nausea or abdominal distress.
8. Feeling dizzy, unsteady, light-headed, or faint.
9. Chills or heat sensations.
10. Paresthesias (numbness or tingling sensations).
11. Derealization (feelings of unreality) or depersonalization (being detached from oneself).
12. Fear of losing control or "going crazy."
13. Fear of dying.

Note: Culture-specific symptoms (e.g., tinnitus, neck soreness, headache, uncontrollable screaming or crying) may be seen. Such symptoms should not count as one of the four required symptoms.

B. At least one of the attacks has been followed by 1 month (or more) of one or both of the following:

1. Persistent concern or worry about additional panic attacks or their consequences (e.g., losing control, having a heart attack, "going crazy").
2. A significant maladaptive change in behavior related to the attacks (e.g., behaviors designed to avoid having panic attacks, such as avoidance of exercise or unfamiliar situations).

C. The disturbance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition (e.g., hyperthyroidism, cardiopulmonary disorders).

D. The disturbance is not better explained by another mental disorder (e.g., the panic attacks do not occur only in response to feared social situations, as in Social Anxiety Disorder: in response to circumscribed phobic objects or situations, as in specific Phobia: in response to obsessions, as in Obsessive-Compulsive Disorder: in response to reminders of traumatic events, as in Post-Traumatic Stress Disorder: or in response to separation from attachment figures, as in Separation Anxiety Disorder)."

Panic Attack Specifier

"Note: Symptoms are presented for the purpose of identifying a panic attack; however, panic attack is not a mental disorder and cannot be coded. Panic attacks can occur in the context of any anxiety disorder as well as other mental disorders (e.g., depressive disorders, posttraumatic stress disorder, substance use disorders) and some medical conditions (e.g., cardiac, respiratory, vestibular, gastrointestinal). When the presence of a panic attack is identified, it should be noted as a specifier (e.g., "posttraumatic stress disorder with panic attacks"). For panic disorder, the presence of panic attack is contained within the criteria for the disorder and panic attack is not used as a specifier.

An abrupt surge of intense fear or intense discomfort that reaches a peak within minutes, and during which time four (or more) of the following symptoms occur:

Note: The abrupt surge can occur from a calm state or an anxious state.

1. Palpitations, pounding heart, or accelerated heart rate.
2. Sweating.
3. Trembling or shaking.
4. Sensations of shortness of breath or smothering.
5. Feelings of choking.
6. Chest pain or discomfort.
7. Nausea or abdominal distress.
8. Feeling dizzy, unsteady, light-headed, or faint.
9. Chills or heat sensations.
10. Paresthesias (numbness or tingling sensations).
11. Derealization (feelings of unreality) or depersonalization (being detached from oneself).
12. Fear of losing control or "going crazy."
13. Fear of dying.

Note: Culture-specific symptoms (e.g., tinnitus, neck soreness, headache, uncontrollable screaming or crying) may be seen. Such symptoms should not count as one of the four required symptoms."

Specific Phobia

“A. Marked fear or anxiety about a specific object or situation (e.g., flying, heights, animals, receiving an injection, seeing blood).

Note: In children, the fear or anxiety may be expressed by crying, tantrums, freezing, or clinging.

- B. The phobic object or situation almost always provokes immediate fear or anxiety.
- C. The phobic object or situation is actively avoided or endured with intense fear or anxiety.
- D. The fear or anxiety is out of proportion to the actual danger posed by the specific object or situation and to the sociocultural context.
- E. The fear, anxiety, or avoidance is persistent, typically lasting for 6 months or more.
- F. The fear, anxiety, or avoidance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- G. The disturbance is not better explained by the symptoms of another mental disorder, including fear, anxiety, and avoidance of situations associated with panic-like symptoms or other incapacitating symptoms (as in Agoraphobia); objects or situations related to obsessions (as in Obsessive-Compulsive Disorder); reminders of traumatic events (as in Post-Traumatic Stress Disorder); separation from home or attachment figures (as in Separation Anxiety Disorder); or social situations (as in Social Anxiety Disorder).”¹

Agoraphobia

“A. Marked fear or anxiety about two (or more) of the following five situations:

- 1. Using public transportation (e.g., automobiles, buses, trains, ships, planes).
- 2. Being in open spaces (e.g., parking lots, marketplaces, bridges).
- 3. Being in enclosed places (e.g., shops, theaters, cinemas).
- 4. Standing in line or being in a crowd.
- 5. Being outside of the home alone.

B. The individual fears or avoids these situations because of thoughts that escape might be difficult or help might not be available in the event of developing panic-like symptoms or other incapacitating or embarrassing symptoms (e.g., fear of falling in the elderly; fear of incontinence).

¹ Text has been directly quoted from the American Psychiatric Association’s *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5). Specific diagnostic terms have been capitalized in these text quotations in this section.

- C. The agoraphobic situations almost always provoke fear or anxiety.
- D. The agoraphobic situations are actively avoided, require the presence of a companion, or are endured with intense fear or anxiety.
- E. The fear or anxiety is out of proportion to the actual danger posed by the agoraphobic situations and to the sociocultural context.
- F. The fear, anxiety, or avoidance is persistent, typically lasting for 6 months or more.
- G. The fear, anxiety, or avoidance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- H. If another medical condition (e.g., inflammatory bowel disease, Parkinson's disease) is present, the fear, anxiety, or avoidance is clearly excessive.
- I. The fear, anxiety, or avoidance is not better explained by the symptoms of another mental disorder—for example, the symptoms are not confined to specific phobia, situational type; do not involve only social situations (as in Social Anxiety Disorder); and are not related exclusively to obsessions (as in Obsessive-Compulsive Disorder), perceived defects or flaws in physical appearance (as in Body Dysmorphic Disorder), reminders of traumatic events (as in Post-Traumatic Stress Disorder), or fear of separation (as in Separation Anxiety Disorder).

Note: Agoraphobia is diagnosed irrespective of the presence of Panic Disorder. If an individual's presentation meets criteria for Panic Disorder and Agoraphobia, both diagnoses should be assigned."

Substance/Medication-Induced Anxiety Disorder

- "A. Panic attacks or anxiety is predominant in the clinical picture.
- B. There is evidence from the history, physical examination, or laboratory findings of both (1) and (2):
 - 1. The symptoms in Criterion A developed during or soon after substance intoxication or withdrawal or after exposure to a medication.
 - 2. The involved substance/medication is capable of producing the symptoms in Criterion A.
- C. The disturbance is not better explained by an anxiety disorder that is not substance/medication induced. Such evidence of an independent anxiety disorder could include the following:
 - The symptoms precede the onset of the substance/medication use; the symptoms persist for a substantial period of time (e.g., about 1 month) after the cessation of acute withdrawal or severe intoxication; or there is other evidence suggesting the existence of an independent non-substance/medication-induced anxiety disorder (e.g., a history of recurrent non-substance/medication-related episodes).
- D. The disturbance does not occur exclusively during the course of a delirium.

E. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Note: This diagnosis should be made instead of a diagnosis of substance intoxication or substance withdrawal only when the symptoms in Criterion A predominate in the clinical picture and they are sufficiently severe to warrant clinical attention.”

Anxiety Disorder Due to Another Medical Condition

“A. Panic attacks or anxiety is predominant in the clinical picture.

B. There is evidence from the history, physical examination, or laboratory findings that the disturbance is the direct pathophysiological consequence of another medical condition.

C. The disturbance is not better explained by another mental disorder.

D. The disturbance does not occur exclusively during the course of a delirium.

E. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.”

ICD-10 Criteria

Generalized Anxiety Disorder

Generalized anxiety persistent but not restricted to particular environmental circumstances. Symptoms vary but can include complaints of persistent nervousness, trembling, muscular tensions, sweating, lightheadedness, palpitations, dizziness, and epigastric discomfort. Also common are fears that the individual or a relative will become ill or have an accident.

Panic Disorder [Episodic Paroxysmal Anxiety]

Disorder where recurrent attacks of severe anxiety, or panic. Attacks are not restricted to any particular situation or circumstances. Symptoms include sudden onset of palpitations, chest pain, choking sensations, dizziness, and feelings of unreality (depersonalization or derealization). Secondary fear of dying, losing control, or going mad can also occur. Panic disorder may be secondary to depression if the patient has a depressive disorder when attacks start.

Phobic Anxiety Disorders

Group of disorders of which anxiety is evoked in certain well-defined situations that are not dangerous. Avoidance or approaching situations with dread occurs, which can lead to anticipatory anxiety. Symptoms such as palpitations, feeling faint, secondary fears of dying, losing control, or going mad.

Social Phobias

Avoidance of social interactions or situations due to fear of scrutiny from others. Can be associated with low self-esteem, fear of criticism, blushing, hand tremor, nausea, or urgency of micturition. Symptoms can develop into panic attacks.

Specific (Isolated) Phobias

Phobias that occur predominately to specific situations (e.g., proximity to certain animals, heights, flying, darkness, medical procedures, etc.). Proximity to these situations or objects can lead to panic.

Agoraphobia

Phobias characterized by fears of leaving home, crowds and public places, or traveling alone in public transportation. Present and past episodes commonly feature panic disorder. Other common signs include depression and/or obsessional symptoms, social phobias, avoidance of phobic situations

Other Anxiety Disorders

These include disorders in which anxiety is the major symptom. Anxiety is not restricted to any particular environmental situation. Secondary or less severe depression or obsessional symptoms may be present.

Mixed Anxiety and Depressive Disorder

Symptoms of anxiety and depression both present, but neither predominant nor present enough to justify a diagnosis if considered separately.

Screening and Testing Recommendations

Medical and pharmaceutical causes of anxiety disorders should be ruled out and/or addressed (e.g., hyperthyroidism, other endocrine disorders, cardiac disorders, dysrhythmias, pulmonary disorders, stimulant use, marijuana).

There are numerous screening tools and psychometric tests. Screening tools generally include few items, emphasize high sensitivity, and require less education to administer.

Although screening tools generally do not have secure item pools, standardized tests generally do. Additionally, psychometric tests may have specific administration protocols that must be followed, have greater specificity, and require professionally trained mental health professionals to administer. While these instruments may suggest a diagnosis, neither screening tools nor psychometric tests alone can make a diagnosis. The diagnosis should only be concluded after careful analysis of all available data, including from a thorough history and/or clinical interview. Additionally, measures have versions with differing lengths (e.g., PHQ-9 and PHQ-2 measures of depression). In general, although shorter measures place less burden

on the patient, shorter measures may suffer from reduced sensitivity, specificity, reliability, and other problems.

Anxiety Disorders Screening Tools

There are many anxiety disorders screening tools. These include the following:

- Beck Anxiety Inventory (BAI) [17, 350-358]
 - Both free and standardized versions available
 - Short administration time
 - Easily hand scored
- Clinically Useful Anxiety Outcome Scale (CUXOS) [359, 360]
 - Free version available
 - Short administration time
 - Easily hand scored
- Generalized Anxiety Disorder-7 (GAD-7) [361-371]
 - Free version available
 - Short administration time
 - Easily hand scored
- Hamilton Anxiety Rating Scale (HAM-A) [372-380]
 - Free version available
 - Filled out by the provider after interviewing the patient
 - Easily hand scored
- PROMIS Anxiety Measures [381-392]
 - Free version available
 - Short administration time
 - Easily hand scored
- State-Trait Anxiety Inventory [393-403]
 - Copyrighted standardized test
- Symptom Checklist 90 Revised (SCL-90/SCL-90-R) [404-413]
 - 90-item scale with 12 scales, which includes measures of anxiety and phobias
 - Copyrighted standardized test
- Brief Symptom Inventory (BSI) [414-417]
 - Shorter 53-item version of the SCL-90
 - Copyrighted standardized test
- Brief Symptom Inventory-18 (BSI) [414-417]
 - Shorter 18-item version of the SCL-90 with three scales for anxiety, depression, and somatization
 - Copyrighted standardized test

Anxiety Disorders Screening Tools

Recommended.

The use of anxiety disorders screening tools is moderately recommended.

Strength of Evidence – **Moderately Recommended, Evidence (B)**

Level of Confidence – **Moderate**

<i>Indications:</i>	Patients at risk of or exhibiting symptoms of a possible anxiety disorder. Evaluation should include focus on anxiety disorders, depressive disorder(s), bipolar disorder, substance use disorder(s), and risk of suicide.
<i>Benefits:</i>	Earlier identification of potential anxiety disorders; assists with directing the patient to appropriate mental health services that include diagnostic confirmation.
<i>Harms:</i>	Negligible. False-positive results are the highest risk with a screening tool, although there also is a lower potential for inappropriate assurance for a false-negative result. There also is risk of a false conclusion if a positive screen is inadvertently relied upon for diagnosis without additional testing/confirmation.
<i>Frequency/Dose/Duration:</i>	Generally, only one administration for typical purposes. Shorter version instruments are generally considered superior to longer instruments for purposes of screening primarily due to compliance and incrementally less gain with longer instruments.
<i>Rationale:</i>	There are multiple high- and moderate-quality studies evaluating the efficacy and validity of screening tests for anxiety disorders. However, few studies compare multiple screening tests in sizable populations of patients. Some evidence suggests the PHQ-2 may have better discriminant validity [418] and another study suggests that the Brief-PHQ and HADS trend towards better performance than the GHQ-12 [419]. Another study suggested the PHQ-4 was better than the PHQ-2 and GAD-2 [420]. No quality comparative trials that simultaneously assessed numerous screening tools to provide high-quality evidence of comparable utility were identified. Screening tests have no cost and are recommended for the initial screening of patients with potential anxiety disorders.
<i>Evidence:</i>	A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Beck Anxiety Inventory; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; psychology inventory, psychology screening, psychological inventory, psychological screening; not pediatric and not adolescents. We found and reviewed 2683 articles in PubMed using the most recent sorting function. We conducted a secondary review in PubMed using the best match sorting function and found and reviewed 2683 articles. We also found and reviewed 31274 in Scopus, 1442 in CINAHL, 2692 in Cochrane Library, 114000 in Google Scholar, and 1 from other sources. We considered for inclusion 2 from PubMed, 2 from Scopus, 1 from CINAHL, 2 from Cochrane Library, 3 from Google Scholar, and 1 from other sources. Of the 11 articles considered for inclusion, 11 diagnostic studies and 0 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Brief Symptom Inventory; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; psychology inventory, psychology screening, psychological inventory, psychological screening; not pediatric and not adolescents. We found and reviewed 428 articles in PubMed using the most recent sorting function. We conducted a secondary review in PubMed using the best match sorting function and found and reviewed 816 articles. We also found and reviewed 788 in Scopus, 615 in CINAHL, 32 in Cochrane Library, 127,000 in Google Scholar, and 0 from other sources. We considered for inclusion 1 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 0 from other sources. Of the 4 articles considered for inclusion, 2 diagnostic studies and 0 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Clinically Useful Anxiety Outcome Scale; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; psychology inventory, psychology screening, psychological inventory, psychological screening; not pediatric and not adolescents. We found and reviewed 18 articles in PubMed using the most recent sorting function. We conducted a secondary review in PubMed using the best match sorting function and found and reviewed 125 articles. We also found and reviewed 20 in Scopus, 0 in CINAHL, 40 in Cochrane Library, 79,900 in Google Scholar, and 3 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 3 from other sources. Of the 3 articles considered for inclusion, 3 diagnostic studies and 0 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Generalized Anxiety Disorder Scale-7, GAD-7; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; psychology inventory, psychology screening, psychological inventory, psychological screening; not pediatric and not adolescents. We found and reviewed 1040 articles in PubMed using the most recent sorting function. We conducted a secondary review in PubMed using the best match sorting function and found and reviewed 1080 articles. We also found and reviewed 12 in Scopus, 135 in CINAHL, 9 in Cochrane Library, 7200 in Google Scholar, and 10 from other sources. We considered for inclusion 5 from PubMed, 1 from Scopus, 2 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 10 from other sources. Of the 18 articles considered for inclusion, 13 diagnostic studies and 3 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date

limits using the following terms: Hamilton Anxiety Rating Scale, HAM-A; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; psychology inventory, psychology screening, psychological inventory, psychological screening; not pediatric and not adolescents. We found and reviewed 827 articles in PubMed using the most recent sorting function. We conducted a secondary review in PubMed using the best match sorting function and found and reviewed 884 articles. We also found and reviewed 348 in Scopus, 7330 in CINAHL, 75 in Cochrane Library, 32100 in Google Scholar, and 1 from other sources. We considered for inclusion 8 from PubMed, 0 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 10 articles considered for inclusion, 6 diagnostic studies and 0 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Patient Health Questionnaire, PHQ; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; psychology inventory, psychology screening, psychological inventory, psychological screening; not pediatric and not adolescents. We found and reviewed 288 articles in PubMed using the most recent sorting function. We conducted a secondary review in PubMed using the best match sorting function and found and reviewed 368 articles. We also found and reviewed 442 in Scopus, 3 in CINAHL, 1 in Cochrane Library, 23800 in Google Scholar, and 2 from other sources. We considered for inclusion 12 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 3 from Google Scholar, and 2 from other sources. Of the 18 articles considered for inclusion, 13 diagnostic studies and 0 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: State Trait Anxiety Inventory, STAI; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; psychology inventory, psychology screening, psychological inventory, psychological screening; not pediatric and not adolescents. We found and reviewed 3426 articles in PubMed using the most recent sorting function. We conducted a secondary review in PubMed using the best match sorting function and found and reviewed 3640 articles. We also found and reviewed 5037 in Scopus, 2045 in CINAHL, 1475 in Cochrane Library, 98300 in Google Scholar, and 3 from other sources. We considered for inclusion 8 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 3 from other sources. Of the 12 articles considered for inclusion, 6 diagnostic studies and 0 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Symptom Checklist, Symptom Checklist 90-Revised, SCL-90-R; anxiety, anxiety disorders, panic

disorder, phobic disorder, phobic disorders, phobia; psychology inventory, psychology screening, psychological inventory, psychological screening; not pediatric and not adolescents. We found and reviewed 679 articles in PubMed using the most recent sorting function. We conducted a secondary review in PubMed using the best match sorting function and found and reviewed 699 articles. We also found and reviewed 372 in Scopus, 161 in CINAHL, 74 in Cochrane Library, 8,080 in Google Scholar, and 2 from other sources. We considered for inclusion 7 from PubMed, 1 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 2 from other sources. Of the 12 articles considered for inclusion, 10 diagnostic studies and 0 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens, then the remaining articles are not reviewed due to a lack of relevancy.

Psychometric Testing

Several psychometric tests are commonly used for the evaluation of patients with potential anxiety disorders. Examples include the Millon Clinical Multiaxial Inventory-IV (MCMI-IV), Personality Assessment Inventory (PAI), Battery for Health Improvement 2nd Edition, the Minnesota Multiphase Personality Inventory (MMPI)-2 and MMPI-2-RF [429-436]. See also the general approach to psychometric testing in the [Workplace Mental Health Introduction](#). Psychometric testing often follows a positive result from a screening test.

In the psychological assessment of anxiety, although an anxiety screening tool is intended to detect the presence of anxious symptoms, a psychological inventory is intended to survey a broad range of biopsychosocial symptoms and provide a context within which the anxiety symptoms can be interpreted. For example, for a patient with a screen that is positive for anxiety, the interpretation of the anxiety is different depending on whether it occurs within the context of psychological trauma, chronic generalized anxiety, panic disorder, obsessive-compulsive disorder, hypomania, medical phobias, excessive caffeine use, or impending bankruptcy. Thus, in the occupational psychological evaluation, there is not a one-to-one relationship between a scale score and a diagnosis or treatment plan, as anxiety symptoms may be associated with different etiologies. Understanding the etiology of the anxious symptoms is essential to the determination of its cause and the development of an effective treatment plan. For example, for a patient with a high anxiety score, the treatment plan would differ if the anxiety was associated with a workplace trauma, as opposed to being associated with caffeine abuse or a history of chronic generalized anxiety.

There are multiple studies evaluating the usage of psychometric testing and subscales for identifying elements of psychosis within mixed psychiatric patients, including those with anxiety

disorders, depressive disorders, PTSD, and/or substance abuse disorders [437-468]. Additional studies evaluated usage for community samples such as veterans, college students, etc. [464, 469-477], fitness-for-duty evaluations [478], chronic pain patients [479, 480], injured workers and personal injury litigations [453, 481-489], within forensic evaluations or criminal settings [446, 490-497], and differentiating between true participants and simulators (malingering participants, either trained or untrained) [480, 486, 498-509].

Psychometric Testing

Recommended.

The use of psychometric testing is moderately recommended for anxiety disorders.

Strength of Evidence – Moderately Recommended, Evidence (B)

Level of Confidence – Moderate

<i>Indications:</i>	For individuals presenting with signs and symptoms consistent with an anxiety disorder. May have tested positive with a prior anxiety disorder screening test. Evaluation should especially include focus on various anxiety disorders, depressive disorder(s), bipolar disorder, substance use disorder(s), and risk of suicide.
<i>Benefits:</i>	Provide psychometric evidence regarding potential for anxiety disorders and especially for other mental health disorder(s).
<i>Harms:</i>	Negligible
<i>Frequency/Dose/Duration:</i>	One-time testing unless otherwise indicated (e.g., by subsequent recurrence of or significant changes in symptoms). Requires administration by a professionally trained mental health professional, usually a psychologist [510-512].
<i>Rationale:</i>	There are multiple moderate-quality studies suggesting utility of psychometric testing for anxiety disorders, although there are no large studies comparing all psychometric tests against a gold standard of clinical impression to ascertain which perform the best. The MMPI-2 has been suggested to be able to (1) distinguish anxiety and (2) differentiate between true anxiety and simulators [436]. Data also suggest discriminatory ability of the Millon Clinical Multiaxial Inventory II [513] [434, 435]. Psychometric testing has negligible adverse effects, is moderately costly, and is recommended for assisting in the diagnosis of anxiety disorders. Clinical correlation is required [444].
<i>Evidence:</i>	A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Brief Battery for Health Improvement, BBHI2; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; psychology inventory, psychology screening, psychological inventory, psychological screening; sensitivity and specificity, reproducibility of results; not pediatric and not adolescents. We found and reviewed 5 articles in PubMed using the most recent sorting function. We conducted a secondary review in PubMed using the best match sorting function and found and reviewed 8 articles. We also found and reviewed 3 in Scopus, 0 in CINAHL, 0 in Cochrane Library, 5690 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from

Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Battery for Health Improvement, BHI; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; psychology inventory, psychology screening, psychological inventory, psychological screening; not pediatric and not adolescents. We found and reviewed 56 articles in PubMed using the most recent sorting function. We conducted a secondary review in PubMed using the best match sorting function and found and reviewed 56 articles. We also found and reviewed 655 in Scopus, 2 in CINAHL, 0 in Cochrane Library, 336 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Personality Assessment Inventory, PAI, Personality Assessment; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; psychology inventory, psychology screening, psychological inventory, psychological screening; not pediatric and not adolescents. We found and reviewed 1,841 articles in PubMed using the most recent sorting function. We conducted a secondary review in PubMed using the best match sorting function and found and reviewed 1,841 articles. We also found and reviewed 27,766 in Scopus, 298 in CINAHL, 12 in Cochrane Library, 20,100 in Google Scholar, and 1 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 1 from other sources. Of the 4 articles considered for inclusion, 4 diagnostic studies and 0 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Millon Clinical Multiaxial Inventory, MCMI; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; psychology inventory, psychology screening, psychological inventory, psychological screening; not pediatric and not adolescents. We found and reviewed 66 articles in PubMed using the most recent sorting function. We conducted a secondary review in PubMed using the best match sorting function and found and reviewed 66 articles. We also found and reviewed 63 in Scopus, 1 in CINAHL, 0 in Cochrane Library, 3,240 in Google Scholar, and 0 from other sources. We considered for inclusion 2 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 2 articles considered for inclusion, 2 diagnostic studies and 0 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Minnesota Multiphasic Personality Inventory, MMPI; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; psychology inventory, psychology screening, psychological inventory, psychological screening; not pediatric and not adolescents. We found and reviewed 649 articles in PubMed using the most recent sorting function. We conducted a secondary review in PubMed using the best match sorting function and found and reviewed 649 articles. We also found and reviewed 1,702 in Scopus, 146 in CINAHL, 77 in Cochrane Library, 22,800 in Google Scholar, and 2 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 2 from other sources. Of the 3 articles considered for inclusion, 3 diagnostic studies and 0 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Pharmacogenomics Testing

Pharmacogenomic testing has been used to guide psychiatric treatment based on the person's pharmacogenomics genotype to determine how the patient will respond to antidepressants and guide psychiatric treatment [515-520].

Pharmacogenomics Testing

No Recommendation.

There is no recommendation regarding the use of pharmacogenomics testing for anxiety disorders.

Strength of Evidence – No Recommendation, Insufficient Evidence (I)

Level of Confidence – Low

Rationale:

One RCT suggested both anxiety and depression patients had better clinical outcomes from treatment based on pharmacogenomics testing [521]. However, another RCT evaluating the use of pharmacogenomics testing that included patients with anxiety among other disorders [517] found no changes in outcomes, although adverse effects were lower. Thus, there is no recommendation. Pharmacogenomic testing is minimally invasive, has low adverse effects, but is moderate cost; thus, there is no recommendation as there was no clear efficacy in a single study. These tests may have some utility for anxiety patients who are

Evidence:

refractory to usual treatments and/or are intolerant of multiple medication trials.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Pharmacogenomic testing, Pharmacokinetic Testing; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; diagnosis, diagnostic, sensitivity, specificity, positive predictive value, negative predictive value, predictive value of tests, efficacy, efficiency; not pediatric and not adolescents. We found and reviewed 18 articles in PubMed using Most Recent tab, and we did a secondary search in PubMed using Best Match tab to find and review 236 articles, 68 in Scopus, 1 in CINAHL, 50 in Cochrane Library, 4310 in Google Scholar, and 0 from other sources†. We considered for inclusion 1 from PubMed, 3 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 0 from other sources. Of the 6 articles considered for inclusion, 1 diagnostic study and 2 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Treatment Recommendations

Education

Education training for anxiety disorders typically involves teaching information and specific skills to assist in coping with symptoms of anxiety. Educational programs use various methods including online training and targeted training to conduct motivational interviewing, teach goal setting, and assign behavioral tasks. It is often used in conjunction with treatments, such as CBT, exercise, and/or anxiolytic medications.

Education

Recommended.

Education is recommended for the treatment of patients with anxiety disorders.

Strength of Evidence – Recommended, Insufficient Evidence (I)

Level of Confidence – Moderate

Indications:

Individuals with anxiety or symptoms of a potential anxiety disorder

Benefits:

Improved understanding and/or resolution and/or improvement of symptoms

Harms:

Negligible

<i>Frequency/Dose/Duration:</i>	Typically at least one formal teaching session, often in conjunction with the initiation of treatment, with subsequent education based on response to treatment, severity, patient's knowledge, and retention. Education may include information about the disorder, treatment, importance of exercise, self-care, work and leisure. Professions delivering quality education for anxiety disorders varies widely, and the accuracy and precision for the given patient is believed to be quite important.
<i>Indications for Discontinuation:</i>	Sufficient understanding of anxiety, resolution of symptoms, non-compliance.
<i>Rationale:</i>	There are no quality trials that have relied on education as the primary intervention for anxiety disorders. There is one moderate-quality trial that assessed education combined with CBT compared with aerobic exercise plus CBT and found the exercise arm to be inferior [522]. Another trial found an educational supportive group therapy to be inferior to either CBT or phenelzine for social phobia [523]. Yet, education is naturally included in many trials, including likely most that did not mention education in the publication, as education is generally important to gain acceptance, treatment compliance, and prevent dropouts in trials utilizing any of the various therapies assessed. Education may be helpful for patient understanding, likely improves patient compliance with interventions and thus is recommended.
<i>Evidence:</i>	A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Education; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 3639 articles in PubMed, 21074 in Scopus, 2756 in CINAHL, 0 in Cochrane Library, 260000 in Google Scholar, and 0 from other sources [†] . We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

[†] The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Activity Modification and Exercise

Exercise has been used to treat anxiety [522, 524-564].

Exercise

Recommended.

Aerobic exercise is moderately recommended for the treatment of patients with anxiety disorders. Strengthening exercise is also recommended. A flexibility-based exercise program is not recommended.

Strength of Evidence – Moderately Recommended, Evidence (B) – Aerobic Exercise

Level of Confidence – Moderate

Strength of Evidence – Recommended, Insufficient Evidence (I) – Strengthening

Level of Confidence – Low

Strength of Evidence – Not Recommended, Evidence (C) – Flexibility-based Exercise

Level of Confidence – Low

Indications:

Anxiety symptoms sufficient to warrant treatment. Aerobic exercise is often combined with CBT [522, 547, 565]. Other first-line treatments include non-addictive anxiolytics. Strengthening/resistive exercises may be selectively used for particularly motivated patients, although the evidence for efficacy of aerobic exercises is considerably stronger. Improvement in anxiety symptoms, reduced panic attacks, increased physical function, and overall well-being. Durability and ongoing improvement after cessation of formal treatment has also been reported [547].

Benefits:

Harms:

Negligible, muscle soreness

Frequency/Dose/Duration:

The highest-quality trial used a treadmill for 30 minutes, 3 times a week for 8 weeks [547]. One trial targeted exercise sessions at 60–80% of maximum heart rate for an hour [542]. Quality data suggest superiority of aerobic over flexibility exercises [547].

Indications for Discontinuation:

Resolution of anxiety symptoms, panic attacks, non-compliance, or unanticipated adverse event.

Rationale:

The highest-quality study found aerobic exercise plus CBT was superior to flexibility and exercises with little muscle strain among patients with panic disorder; the differences were particularly pronounced by 7 months, also suggesting durability of the effects after the cessation of formal training on anxiety [547]. Another moderate-quality trial found both CBT and exercise were effective, although the CBT was more effective [542]. A trial of adjunctive moderate vs. low aerobic exercise (70% vs. 30% VO_{2Max}) as an adjunct to CBT reported a trend in favor of moderate-intensity exercise [565].

One trial reported comparable results between aerobic exercise and resistance training (lower-body weightlifting) when compared with a waitlist control [539]. There are no other quality strengthening exercise trials.

As there is evidence aerobic exercise is superior to an exercise program that is primarily based on flexibility or range-of-motion exercises, a flexibility-based program is without evidence-based support, particularly absent material, functional range-of-motion deficits [547].

Aerobic exercise plus CBT has been associated with improved symptoms of anxiety over education plus CBT [522]. Exercise has low adverse effects; is of low to moderate cost depending upon whether self-directed, group sessions, or via a personal trainer; nearly consistently shows efficacy; and thus is recommended for treatment of anxiety disorders. Flexibility-based programs appear unwarranted as they are without evidence of efficacy.

Evidence:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: exercise, physical activity, acute exercise, isometric exercise, aerobic exercise, exercise training; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 725 articles in PubMed, 10518 in Scopus, 330 in CINAHL, 298 in Cochrane Library, 72200 in Google Scholar, and 3 from other sources[†]. We considered for inclusion 16 from PubMed, 6 from Scopus, 7 from CINAHL, 7 from Cochrane Library, 4 from Google Scholar, and 3 from other sources. Of the 43 articles considered for inclusion, 19 randomized trials and 9 systematic reviews met the inclusion criteria.

[†] The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Yoga has been used to treat occupational anxiety [572-585].

Yoga

Recommended.

Yoga is selectively recommended for the treatment of patients with anxiety disorders.

Strength of Evidence – Recommended, Insufficient Evidence (I)

Level of Confidence – Low

<i>Indications:</i>	Anxiety symptoms sufficient to require therapy. Generally should have tried and adhered to an aerobic exercise program first, as evidence of efficacy is stronger for aerobic and then for strengthening exercise.
<i>Benefits:</i>	Improvements in symptoms of anxiety. Increased flexibility, posture, and overall well-being.
<i>Harms:</i>	Negligible, muscle soreness
<i>Frequency/Dose/Duration:</i>	Twice-weekly, 1-hour sessions of yoga for 2 months; results were better if combined with a comparable schedule of CBT [580].
<i>Indications for Discontinuation:</i>	Lack of anxiety symptom improvement or sufficient improvement to not warrant further sessions, noncompliance, intolerance.
<i>Rationale:</i>	There is one low-quality RCT suggesting a combination of Hatha yoga (postures, breathing techniques, relaxation, and meditation) plus CBT was superior to yoga alone for management of anxiety symptoms, particularly including panic disorder [580]. There are multiple trials of mindfulness and/or meditation [574, 575, 577] (see Meditation, Mindfulness, and Relaxation). Yoga has negligible adverse effects, is low to moderate cost (depending on whether self-directed or supervised), but is of questionable efficacy; therefore, there is a limited recommendation for use among those who trialed and adhered to aerobic exercise and/or had insufficient benefits and/or have particular motivation to comply with yoga.
<i>Evidence:</i>	A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: yoga; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed articles in 264 PubMed, 1,456 in Scopus, 256 in CINAHL, 87 in Cochrane Library, 15,300 in Google Scholar, and 0 from other sources†. We considered for inclusion 7 from PubMed, 2 from Scopus, 2 from CINAHL, 0 from Cochrane Library, 3 from Google Scholar, and 0 from other sources. Of the 14 articles considered for inclusion, 4 randomized trials and 9 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens, then the remaining articles are not reviewed due to a lack of relevancy.

Behavioral and Psychological Interventions

Many types of cognitive behavioral therapy (CBT) have been used to treat anxiety [277, 522, 523, 542, 553, 580, 586-698]. Bibliotherapy has been used to treat anxiety [696, 699-721] as part of CBT, as has acceptance and commitment therapy [692, 722-746]. Interpersonal therapy has also been used for treatment of anxiety [6, 670, 694, 697, 698, 747-751]. Some cognitive therapies have been administered using technology [592, 600, 629, 637, 641, 659, 706, 708, 714, 715, 719, 752-797]. The treatment of panic disorder is unique in that it is associated with crises and increased usage of hospital emergency department (ED) services. If ED overutilization is present, a crisis management plan may be necessary prior to initiating cognitive or other longer-term psychotherapies.

Cognitive Behavioral Therapy

Moderately Recommended.

Cognitive behavioral therapy is moderately recommended for the treatment of patients with anxiety disorders.

Strength of Evidence – Moderately Recommended, Evidence (B)

Level of Confidence – High

Computer-Assisted Cognitive Behavioral Therapy

Moderately Recommended.

The use of computer-assisted cognitive behavioral therapy and cognitive behavioral stress management is moderately recommended for the treatment of patients with anxiety disorders.

Strength of Evidence – Moderately Recommended, Evidence (B)

Level of Confidence – Moderate

Bibliotherapy/Cognitive Behavioral Therapy Bibliotherapy

Recommended.

The use of bibliotherapy/cognitive bibliotherapy is recommended for the treatment of patients with anxiety disorders.

Strength of Evidence – Recommended, Evidence (C)

Level of Confidence – Low

Dialectical Behavior Therapy

No Recommendation.

There is no recommendation for the use of dialectical behavior therapy for the treatment of patients with anxiety disorders.

Strength of Evidence – No Recommendation, Insufficient Evidence (I)

Level of Confidence – Low

Acceptance and Commitment Therapy

Moderately Recommended.

The use of acceptance and commitment therapy is moderately recommended for the treatment of patients with anxiety disorders.

Strength of Evidence – Moderately Recommended, Evidence (B)

Level of Confidence – Moderate

Interpersonal Therapy

Recommended.

The use of interpersonal therapy is recommended for the treatment of patients with anxiety disorders.

Strength of Evidence – Recommended, Insufficient Evidence (I)

Level of Confidence – Low

CBT Combined with Antidepressants

Moderately Recommended.

The combined use of CBT and antidepressants is moderately recommended for the treatment of patients with anxiety disorders, especially social anxiety disorder and panic disorder.

Strength of Evidence – Moderately Recommended, Evidence (B)

Level of Confidence – Low

Indications:

An anxiety disorder sufficient to require treatment. CBT is often first-line treatment and may be used in addition to aerobic exercise and strengthening exercise. CBT may be used with medication for severe cases where CBT is generally adjunctive, rather than a stand-alone treatment.

Benefits:

There is quality evidence suggesting efficacy of combined CBT and escitalopram for social anxiety disorder [766]. CBT plus escitalopram was superior to CBT alone for social anxiety disorder [766]. CBT plus phenelzine has been found to be superior to each treatment alone [593] and another trial found phenelzine superior to CBT [523]. One trial found comparable efficacy between CBT and paroxetine for treatment of panic disorder [632], whereas another suggested the combination of imipramine plus CBT to be superior to either drug alone for panic disorder, although CBT was more efficacious sooner [591].

Improvement in anxiety symptoms

Harms:

Infrequent and negligible

Frequency/Dose/Duration:

Variable regimens have been used. Internet-based strategies have been shown to be equally efficacious and more cost-effective (see Rationale below). Different distance-based regimens have been used, including completion of an 8-week course [765] and completion of a series of 10–12 modules [708, 767]. The number of in-person sessions used has ranged in the studies from approximately 5–10 one-hour sessions [678], with one trial including up to 30 sessions [642].

Indications for Discontinuation:

Symptom resolution, non-compliance, lack of efficacy, or adverse effects.

Rationale:

There are many types of CBT and many moderate-quality studies suggesting efficacy of CBT for anxiety disorders. However, quality evidence for any specific CBT type is variable, ranging from good to insufficient. CBT components with quality evidence allowing evidence-based guidance include computer-assisted cognitive behavioral therapy, cognitive bibliotherapy, and acceptance and commitment therapy.

Internet-based CBT has been repeatedly shown to be either at least as effective as traditional CBT or to be successful when compared to other treatment conditions [592, 600, 637, 641, 706, 708, 714, 715, 753, 765, 767, 769-772, 774, 776, 777, 779, 780, 784, 798, 799] with persistence of positive results reported as long as 3 years [775, 783]. One trial found therapist guidance to be superior to unguided treatment [778], while another reported no differences [736], and still another reported a trained therapist was not essential to effect positive results [772].

Multiple moderate-quality studies suggest efficacy of CBT compared to usual care [277, 635, 661]. However, patient commitment to various CBT programs is necessary for success when treating anxiety and often the studies have high attrition rates. Some studies suggest that CBT reduces or prevents anxiety relapse [277, 574, 643]. In one study, the combination of internet-delivered CBT plus escitalopram was superior to iCBT alone for social anxiety disorder [766]. CBT plus phenelzine has been found to be superior to each treatment alone [593] and another trial found phenelzine superior to CBT [523]. One trial found comparable efficacy between CBT and paroxetine for treatment of panic disorder [632], while another suggested the combination of imipramine plus CBT to be superior to either alone for panic disorder, although CBT was more efficacious sooner [591].

Nearly all quality studies have suggested that interpersonal psychotherapy is inferior to CBT for treatment of anxiety disorders [670, 694, 749, 751]. Dialectical behavior therapy is not generally used for anxiety disorders and the available literature assessing its efficacy includes heterogeneous populations, rather than pure anxiety patients, resulting in no quality evidence of efficacy and thus no recommendation.

Evidence:

CBT has low adverse effects, is of moderate cost depending upon treatment type and duration, and has evidence of efficacy for the treatment of mild to moderate anxiety. Thus, CBT is recommended. A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Cognitive Behavioral Therapy; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic,

systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 2482 articles in PubMed, 12746 in Scopus, 373 in CINAHL, 1278 in Cochrane Library, 189000 in Google Scholar, and 35 from other sources†. We considered for inclusion 83 from PubMed, 18 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 4 from Google Scholar, and 35 from other sources. Of the 142 articles considered for inclusion, 94 randomized trials and 26 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Computer-assisted Cognitive Therapy; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 244 articles in PubMed, 964 in Scopus, 104 in CINAHL, 134 in Cochrane Library, 5050 in Google Scholar, and 15 from other sources†. We considered for inclusion 3 from PubMed, 16 from Scopus, 4 from CINAHL, 6 from Cochrane Library, 16 from Google Scholar, and 15 from other sources. Of the 60 articles considered for inclusion, 47 randomized trials and 13 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: bibliotherapy; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 64 articles in PubMed, 133 in Scopus, 50 in CINAHL, 53 in Cochrane Library, 2530 in Google Scholar, and 0 from other sources†. We considered for inclusion 12 from PubMed, 6 from Scopus, 3 from CINAHL, 1 from Cochrane Library, 2 from Google Scholar, and 0 from other sources. Of the 24 articles considered for inclusion, 17 randomized trials and 2 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Dialectical behavior therapy; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 29 articles in PubMed, 739 in Scopus, 11 in CINAHL, 0 in Cochrane Library, 11500 in Google Scholar, and 0 from other sources†. We considered for inclusion 3 from PubMed, 5 from Scopus, 0 from CINAHL, 0 from Cochrane

Library, 1 from Google Scholar, and 0 from other sources. Of the 9 articles considered for inclusion, 4 randomized trials and 0 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Acceptance and Commitment Therapy; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 157 articles in PubMed, 295 in Scopus, 93 in CINAHL, 109 in Cochrane Library, 34,800 in Google Scholar, and 0 from other sources†. We considered for inclusion 20 from PubMed, 2 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 0 from other sources. Of the 26 articles considered for inclusion, 13 randomized trials and 3 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Interpersonal relations, Interpersonal therapy, Interpersonal psychotherapy, IPT; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 1032 articles in PubMed, 5301 in Scopus, 77 in CINAHL, 217 in Cochrane Library, 37,100 in Google Scholar, and 2 from other sources†. We considered for inclusion 6 from PubMed, 0 from Scopus, 4 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 2 from other sources. Of the 12 articles considered for inclusion, 10 randomized trials and 2 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Insight-oriented therapies have been used to treat anxiety disorders [642, 643, 662, 688-690, 799, 804, 805, 822-833].

Insight-Oriented Therapies (Including Short-Term Psychosocial Psychotherapy)

Recommended.

The use of insight-oriented therapies (including short-term psychosocial psychotherapy) is recommended for the treatment of patients with anxiety disorders.

Strength of Evidence – Recommended, Insufficient Evidence (I)

Level of Confidence – Low

<i>Indications:</i>	Most commonly used for the treatment of panic disorder, although also used for generalized anxiety disorder, typically as a second-line strategy. Should generally have failed treatment with CBT [643, 689]. First-line treatments include CBT (may be done in conjunction), aerobic exercise, strengthening exercise, (re)exposure therapy, and virtual reality.
<i>Benefits:</i>	Improvement in anxiety symptoms
<i>Harms:</i>	Increased symptoms, intolerance
<i>Frequency/Dose/Duration:</i>	One trial used 24 sessions of 50-minute duration, twice weekly for 12 weeks [643].
<i>Indications for Discontinuation:</i>	Resolution of symptoms, non-compliance, lack of efficacy, or adverse events
<i>Rationale:</i>	The panic-focused psychodynamic psychotherapy (PFPP) group and the CBT plus exposure therapy group were comparable in efficacy with a trend towards CBT plus exposure therapy [688]. Another trial found comparable efficacy with CBT [642], although this author also subsequently reported better remission duration with CBT [643]. In another trial, the PFPP group showed a significant reduction in panic severity symptoms (73%) versus the applied relaxation training group (39%) [831]. However, other studies have suggested inferiority to CBT [689] or a lack of efficacy [689]. Insight-oriented therapies have low adverse effects, are low to moderate to high cost depending upon numbers of treatments and treatment duration, have some quality evidence of efficacy, and thus are selectively recommended as a second-line treatment.
<i>Evidence:</i>	A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Insight- Orientated Therapy, psychotherapy brief, psychodynamic, insight oriented therapies, psychodynamic psychotherapy, psychotherapy; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 204 articles in PubMed, 41,113 in Scopus, 60 in CINAHL, 32 in Cochrane Library, 1440 in Google Scholar, and 7 from other sources†. We considered for inclusion 15 from PubMed, 0 from Scopus, 3 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 7 from other sources. Of the 26 articles considered for

inclusion, 15 randomized trials and 2 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Stress inoculation training has been used to treat anxiety disorders [836, 837].

Stress Inoculation Training

No Recommendation.

There is no recommendation for or against the use of stress inoculation training in the treatment of patients with anxiety disorders.

Strength of Evidence – No Recommendation, Insufficient Evidence (I)

Level of Confidence – Low

Rationale:

Evidence:

There are no quality trials and thus no recommendation.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: stress inoculation training, stress inoculation therapy, stress prevention training, stress prevention therapy; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 931 articles in PubMed, 11,719 in Scopus, 8,815,587 in CINAHL, 14 in Cochrane Library, 7540 in Google Scholar, and 0 from other sources†. We considered for inclusion 0 from PubMed, 1 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 2 articles considered for inclusion, 1 randomized trial and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Stress management programs have been used in the treatment of anxiety disorders [795, 838-850].

Stress Management (Behavioral, Cognitive, or Physical)

No Recommendation.

There is no recommendation for stress management as an isolated treatment of patients with anxiety disorders.

Strength of Evidence – No Recommendation, Insufficient Evidence (I)

Level of Confidence – Low

Rationale:

Stress management was inferior to CBT in one trial [795]. Another trial found lack of efficacy for stress management despite having waitlist control bias [840]. A video-delivered relaxation intervention in a pilot study suggested some efficacy, although it was subject to a waitlist control bias [845]. Stress management is not invasive, has low to moderate costs, but the two highest-quality trials suggest lack of efficacy; thus, there is no recommendation for stress management as an isolated intervention.

Evidence:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: cognitive-behavioral stress management, CBSM, cognitive stress management, behavioral stress management, physical stress management, stress management intervention, stress management program; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 1,298 articles in PubMed, 17,430 in Scopus, 78 in CINAHL, 270 in Cochrane Library, 122,000 in Google Scholar, and 7 from other sources[†]. We considered for inclusion 2 from PubMed, 7 from Scopus, 3 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 7 from other sources. Of the 21 articles considered for inclusion, 19 randomized trials and 2 systematic reviews met the inclusion criteria.

[†] The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Supportive therapy has been used to treat anxiety [851-860].

Supportive Therapy

No Recommendation.

There is no recommendation for or against the use of supportive therapy in the treatment of patients with anxiety disorders.

Strength of Evidence – No Recommendation, Insufficient Evidence (I)
Level of Confidence – Low

Rationale:

One trial found CBT to be superior to supportive therapy [523]. Another trial found comparable (in)efficacy of supportive therapy compared with interpersonal therapy [750]. Supportive therapy has low adverse effects and is low cost depending upon treatment duration; however, there is no recommendation as the quality data are sparse and conflicting.

Evidence:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: supportive therapy, psychotherapy, palliative care; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 13,643 articles in PubMed, 7437 in Scopus, 1,082 in CINAHL, 4053 in Cochrane Library, 80,100 in Google Scholar, and 7 from other sources†. We considered for inclusion 2 from PubMed, 4 from Scopus, 0 from CINAHL, 3 from Cochrane Library, 1 from Google Scholar, and 7 from other sources. Of the 18 articles considered for inclusion, 10 randomized trials and 6 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Distractive methods have been used to treat anxiety [861-873].

Distractive Methods

Recommended.

The use of distractive methods is recommended for the treatment of patients with social anxiety and phobia disorders.

Strength of Evidence – Recommended, Evidence (C)

Level of Confidence – Low

<i>Indications:</i>	Most commonly used for situational anxiety (e.g., surgical procedures). Otherwise, distractive methods may be second-line treatment for social anxiety or phobia disorder sufficient to require first-line therapy. Other first-line treatments include CBT (often done in conjunction), aerobic exercise, strengthening exercise, (re)exposure therapy, and virtual reality.
<i>Benefits:</i>	Improvement in anxiety symptoms
<i>Harms:</i>	Increased symptoms, intolerance
<i>Frequency/Dose/Duration:</i>	Most quality studies are single use at the time of a surgical procedure. Otherwise, a few appointments may be reasonable to teach methods for patients where distractive methods may be beneficial. One trial reported that the greatest anxiety reductions were associated with a combination of auditory and visual distractive methods [869].
<i>Indications for Discontinuation:</i>	Resolution of symptoms, non-compliance, lack of efficacy, or adverse events
<i>Rationale:</i>	One trial reported modest efficacy of visual distraction associated with elective colonoscopy [871]. Other trials found efficacy of music distraction compared to relaxation for procedures [865, 868]. Another trial reported lowered pain ratings with distraction (intraoperative talking) and touch, but anxiety ratings were lowered more by music plus intraoperative conversation during conscious surgery [864]. One trial reported the best anxiety reductions were associated with a combination of auditory and visual distractive methods [869]. Distractive methods have low adverse effects, are low cost depending upon treatment duration, and have some studies suggesting efficacy; thus, they are recommended for the treatment of situational anxiety, such as with procedures. Distractive methods may be reasonable for select patients with social anxiety and phobia disorders who are amenable to a few appointments for training regarding their use.
<i>Evidence:</i>	A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Distractive Methods; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 113 articles in PubMed, 4 in Scopus, 21 in CINAHL, 0 in Cochrane Library, 0 in Google Scholar, and 0 from other sources†. We considered for inclusion 8 from PubMed, 0 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 0

from other sources. Of the 36 articles considered for inclusion, 8 randomized trials and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Exposure therapy has been used in the treatment of social anxiety and phobia disorders [565, 595, 603, 604, 683, 691, 797, 874-893].

Exposure Therapy and Prolonged Exposure Therapy Recommended.

The use of exposure therapy or prolonged exposure therapy is recommended for the treatment of patients with social anxiety or phobia disorders.

Strength of Evidence – Recommended, Insufficient Evidence (I) Level of Confidence – Low

<i>Indications:</i>	Social anxiety or phobia disorder sufficient to require first-line therapy. Other first-line treatments include CBT (often done in conjunction), aerobic exercise, and strengthening exercise.
<i>Benefits:</i>	Improvement in anxiety symptoms
<i>Harms:</i>	Increased symptoms, intolerance
<i>Frequency/Dose/Duration:</i>	The highest-quality trial administered 12 weekly treatment sessions with 3 booster sessions after treatment [683].
<i>Indications for Discontinuation:</i>	Resolution of symptoms, non-compliance, lack of efficacy, or adverse events
<i>Rationale:</i>	Exposure therapy was found to be superior to waitlist control and comparable to cognitive behavioral therapy [683]. Another trial found equivalency between VRE and group exposure therapy [891], while another reported equivalency between standard exposure therapy and virtual reality [894]. However, one trial reported cognitive behavioral therapy was superior to combined exposure plus applied relaxation [603]. One trial found no additive benefit of oxytocin [876]. D-cycloserine was not effective as an adjunct to CBT for agoraphobia [884, 885]. There was no additive effect of either yohimbine or propranolol in addition to exposure therapy [895]. Exposure therapy and prolonged exposure therapy have low adverse effects, are moderate cost depending upon treatment duration, and have some studies suggesting efficacy; thus, they are recommended for treatment of social anxiety and phobia disorders.
<i>Evidence:</i>	A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: exposure therapy, behavior exposure therapy, cognitive exposure therapy, implosive therapy, in vivo exposure therapy; anxiety, anxiety disorders, panic disorder, phobic

disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 728 articles in PubMed, 9897 in Scopus, 337 in CINAHL, 108 in Cochrane Library, 319,000 in Google Scholar, and 12 from other sources†. We considered for inclusion 6 from PubMed, 4 from Scopus, 6 from CINAHL, 5 from Cochrane Library, 2 from Google Scholar, and 12 from other sources. Of the 35 articles considered for inclusion, 25 randomized trials and 3 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Virtual reality exposure therapy (VRET) has been used to treat social anxiety and phobia disorders.

Virtual Reality Exposure Therapy Recommended.

The use of virtual reality exposure therapy is recommended for the treatment of patients with social anxiety or phobia disorder.

Strength of Evidence – Recommended, Insufficient Evidence (I) ***Level of Confidence – Low***

<i>Indications:</i>	Social anxiety or phobia disorder sufficient to require first-line therapy. Other first-line treatments include CBT (often done in conjunction), aerobic exercise, and strengthening exercise.
<i>Benefits:</i>	Improvement in anxiety symptoms
<i>Harms:</i>	Increased symptoms, intolerance
<i>Frequency/Dose/Duration:</i>	Appointments and/or self-administered treatments ranged widely, from weekly sessions over 6 weeks [894] to 14 weekly 60-minute sessions [899]. There is no quality evidence to suggest a superior regimen [900]. As there is no evidence of superiority to appointment-based treatments compared with self-administrations, self-administration may be preferable over longer durations for both convenience and cost considerations.
<i>Indications for Discontinuation:</i>	Resolution of symptoms, non-compliance, lack of efficacy, or adverse events
<i>Rationale:</i>	There are no sham-controlled trials. There are many moderate-quality studies that often are subject to waitlist control biases, which have suggested potential efficacy of VRE in the treatment of anxiety disorders. One trial reported augmented reality (combining real world and graphics) inferior to presenting live objects (e.g., spiders), with

Evidence:

differences disappearing at 6 months [901]. VRE was found to be equivalent to standard exposure but superior to wait-list control in another trial [894]. Another trial found equivalency between VRE, computer-aided exposure therapy, and self-administered computer-aided exposure therapy [900]. VRE has low adverse effects, is moderate cost depending upon treatment duration, and has some studies suggesting efficacy; thus, it is recommended for treatment of anxiety disorders with a provoking stimulus (social anxiety or phobia). A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: virtual reality, virtual reality exposure therapy, virtual reality therapy; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 160 articles in PubMed, 941 in Scopus, 131 in CINAHL, 111 in Cochrane Library, 16,300 in Google Scholar, and 0 from other sources†. We considered for inclusion 23 from PubMed, 8 from Scopus, 18 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 0 from other sources. Of the 51 articles considered for inclusion, 29 randomized trials and 15 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Meditation, mindfulness, and relaxation have been used to treat anxiety [574, 577, 638, 646, 654, 689, 690, 701, 773, 831, 839, 868, 919-930].

Meditation, Mindfulness, and Relaxation

Recommended.

Mindfulness therapy is selectively recommended for the treatment of patients with anxiety disorders.

Strength of Evidence – Recommended, Insufficient Evidence (I)

Level of Confidence – Low

Indications:

Individuals with anxiety symptoms. Generally should have been prescribed and adhered to an aerobic exercise program, often after CBT with inadequate results. Meditation/mindfulness and relaxation may be generally better for particularly motivated individuals when used in combination with yoga as well as in addition to aerobic exercise (see [Yoga](#)).

<i>Benefits:</i>	Improvement in anxiety symptoms
<i>Harms:</i>	Negligible
<i>Frequency/Dose/Duration:</i>	Weekly 2.5-hour sessions for 8 weeks of mindfulness therapy [574]
<i>Indications for Discontinuation:</i>	Symptom resolution or lack of efficacy
<i>Rationale:</i>	There is one moderate-quality trial that found cognitive group behavioral therapy was superior to mindfulness-based stress reduction [574]. Two moderate-quality RCTs that are likely subject to wait-list control biases reported some evidence suggesting efficacy of mindfulness-based stress reduction [773, 931]. A moderate-quality trial found lack of efficacy of a brief mindfulness-based stress management program compared with an educational leaflet [850]. A low-quality trial found mindfulness-based stress reduction comparable to an educational control [577], while another by the same author found it superior to an educational control [929]. Another low-quality RCT found mindfulness and acceptance-based group therapy comparable to traditional CBT for social anxiety disorder [924]. Another low-quality trial found mindfulness-based stress reduction comparable to self-directed and unquantified aerobic exercise [575]. Mind/body interventions have low adverse effects, are moderately costly depending upon treatment duration, and have minimal evidence regarding efficacy. Accordingly, meditation, mindfulness and relaxation are selectively recommended for individuals with anxiety symptoms who generally should have been prescribed and adhered to aerobic exercise program, often after CBT with inadequate results; meditation, mindfulness and relaxation may be generally better for motivated individuals when used in combination with yoga as well as in addition to aerobic exercise. There is no recommendation for art therapy, music therapy, or spiritual-based interventions because there is no quality evidence of efficacy.
<i>Evidence:</i>	A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: meditation, mindfulness, relaxation, reflection, contemplation; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 267 articles in PubMed, 23885 in Scopus, 401 in CINAHL, 356 in Cochrane Library, 73900 in Google Scholar, and 14 from other sources†. We considered for inclusion 9 from PubMed, 8 from Scopus, 0 from CINAHL, 1 from Cochrane Library, 2 from Google Scholar, and 14 from other sources. Of the 34 articles considered for inclusion, 20 randomized trials and 7 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens, then the remaining articles are not reviewed due to a lack of relevancy.

Emotional freedom therapy has been used to treat anxiety [604, 933, 934]. Emotional freedom techniques are a form of counseling that incorporates the physical tapping of the body on acupuncture points while simultaneously having the patient focus on traumatic events as a form of self-acceptance therapy.

Emotional Freedom Therapy

No Recommendation.

There is no recommendation for emotional freedom therapy for the treatment of patients with anxiety disorder.

Strength of Evidence – No Recommendation, Insufficient Evidence (I)

Level of Confidence – Low

Rationale:

EFT is a treatment with concerns including lack of a clear underlying theory, lack of quality research, and conflicts of interest [935, 936]. There are no sham-controlled trials. The overall evidence base is quite sparse, with only one small randomized crossover trial which suggested emotional freedom therapy may be effective for reducing phobias due to a specific stimulus. Emotional freedom therapy has quite limited evidence, and thus there is no recommendation.

Evidence:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Emotional Freedom Techniques; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 42 articles in PubMed, 139 in Scopus, in 19 CINAHL, 16 in Cochrane Library, 30,100 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 3 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 3 articles considered for inclusion, 2 randomized trials and 1 systematic review met the inclusion criteria.

[†]The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Medications

Multiple classes of antidepressants and other medications are used to treat anxiety disorders. These include antidepressants, quetiapine, pregabalin, propranolol and hydroxyzine. Benzodiazepines have also been widely used for treatment of anxiety disorders; however, they have considerable problems that include strong addictive potential and being accompanied by withdrawal symptoms. Polypharmacy is a common finding with anxiety disorders and can be particularly problematic in the setting of chronic pain and depression; thus, there is considerable need to avoid benzodiazepines in most of these patients. Instead, consideration of CBT, exercise, and judicious use of non-addictive medications is indicated.

Antidepressant medications are not only a first-line treatment for depression; they are also a first-line treatment for anxiety disorders. These include selective serotonin reuptake inhibitors (SSRIs), selective serotonin and norepinephrine reuptake inhibitors, tricyclic antidepressants, atypical antidepressants, and monoamine oxidase inhibitors.

Antidepressants have been paradoxically used to treat anxiety disorders [523, 524, 570, 591, 593, 632, 636, 656, 800, 801, 803, 806-812, 814, 937-1047].

Antidepressants

Moderately Recommended.

Antidepressants are moderately recommended for the treatment of patients with anxiety disorders.

Strength of Evidence – Moderately Recommended, Evidence (B)

Level of Confidence – Moderate

<i>Indications:</i>	Anxiety disorder sufficient to require medication. May be prescribed in conjunction with other treatments, especially CBT (which had additive benefits in most trials in which it was assessed) [591, 593, 766]. One trial also found additive benefits for clomipramine with aerobic exercise for panic disorder [524].
<i>Benefits:</i>	Improvements in anxiety symptoms, improved function, and reduced relapses.
<i>Harms:</i>	SSRIs (including citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, etc.): Common adverse effects observed for the use of SSRIs can include sleep disturbances, nausea, diarrhea, headache, dizziness, fatigue, and sexual dysfunction. Some patients experience weight gain, increased risk of non-vertebral fractures, or bleeding. Abrupt discontinuation of SSRIs can cause anxiety, mood destabilization, insomnia, dizziness, nausea, vomiting, or even electric-shock sensations [1048]. Citalopram: Restlessness and sleep disturbances, vivid dreams, diarrhea, headache, dizziness, fatigue, sexual dysfunction, weight gain, hyponatremia, possible increased risk of nonvertebral fractures, bleeding. Symptoms of abrupt discontinuation include nervousness, anxiety, irritability, electric-shock sensations, bouts of tearfulness or

crying, dizziness, lightheadedness, insomnia, confusion, trouble concentrating, nausea, vomiting, pregnancy risk class C [320].

Escitalopram: Restlessness and sleep disturbances, vivid dreams, diarrhea, headache, dizziness, fatigue, sexual dysfunction, weight gain, hyponatremia, possible increased risk of nonvertebral fractures, bleeding. Symptoms of abrupt discontinuation include nervousness, anxiety, irritability, electric-shock sensations, bouts of tearfulness or crying, dizziness, lightheadedness, insomnia, confusion, trouble concentrating, nausea, vomiting, pregnancy risk class C [320].

Fluoxetine: More serious adverse effects include worsening of depression, serious allergic reactions, irregular heartbeats, hyponatremia, bleeding, suicidal ideation, and mania in patients with bipolar disorder. Common minor adverse effects include sleepiness, nervousness, insomnia, dizziness, nausea, tremor, skin rash, constipation, upset stomach, loss of appetite, headache, dry mouth, diaphoresis, and weight loss. Abrupt termination of fluoxetine may cause adverse gastrointestinal effects including cramping, nausea, vomiting, diarrhea as well as flu-like symptoms, loss of appetite, lightheadedness, fatigue, headache, dizziness, insomnia, sexual dysfunction, and weight gain. Pregnancy risk class C.

Paroxetine: More serious adverse effects include worsening of depression, serious allergic reactions, irregular heartbeats, hyponatremia, bleeding, suicidal ideation, and mania in bipolar patients. Common minor adverse effects include sleepiness, nervousness, insomnia, dizziness, nausea, tremor, skin rash, constipation, upset stomach, loss of appetite, headache, dry mouth, diaphoresis, and weight loss. Abrupt termination of paroxetine may cause adverse gastrointestinal effects including cramping, nausea, vomiting, and diarrhea, as well as flu-like symptoms, loss of appetite, lightheadedness, fatigue, headache, dizziness, insomnia, sexual dysfunction, and weight gain. Compared to other SSRIs, Paroxetine has a higher incidence of severe withdrawal symptoms due to a shorter relative half-life. Pregnancy risk class D.

Sertraline: Worsening depression, allergic reactions, irregular heartbeat, hyponatremia, bleeding, suicidal ideation as well as mania in bipolar patients. Common minor adverse effects include sleepiness, nervousness, insomnia, dizziness, nausea, tremor, skin rash, constipation, upset stomach, loss of appetite, headache, dry mouth, diaphoresis, and weight loss. Abrupt termination of Sertraline may cause adverse gastrointestinal effects including cramping, nausea, vomiting, diarrhea as well as flu-like symptoms, loss of appetite, lightheadedness, fatigue, headache, dizziness, insomnia, and memory loss.

SNRIs (including duloxetine, desvenlafaxine, milnacipran, reboxetine, venlafaxine, etc.): Common adverse effect is a dose-dependent increase in blood pressure [1048].

Duloxetine: SNRIs can cause a dose-dependent increase in blood pressure [1048]. Common adverse effects of duloxetine include body aches, dry mouth, headache, loss of appetite, nausea, sleepiness, sore throat, sweating increase, or trouble sleeping [1049].

Venlafaxine: Increased sweating, tachycardia, and urinary retention, nausea, vomiting, increased blood pressure. Symptoms of abrupt discontinuation are common especially due to short half-life and include withdrawal symptoms increase in blood pressure, False-positive urine immunoassay screening tests for phencyclidine (PCP) and amphetamine, prolonged QT interval. Pregnancy risk category C [1050].

TCAs (including amoxapine, amineptine, amitriptyline, clomipramine, desipramine, dothiepin, doxepin, imipramine, maprotiline, mianserin, nortriptyline, protriptyline, etc.): Tricyclic antidepressants most commonly cause anticholinergic effects, orthostatic hypotension, weight gain, sedation, and sexual dysfunction. Less common adverse effects include problems with cardiac conduction [1048, 1051]. Tricyclic antidepressants during pregnancy have reported jitteriness and convulsions in newborns [1048]. Some TCAs have been associated with somnolence [1052].

Amitriptyline: sedation, dry mouth, and weight gain [1052, 1053]. In addition, it can cause orthostatic hypotension, sexual dysfunction, and anticholinergic effects such as urinary retention, constipation, blurred vision, and confusion [1052].

Clomipramine: Dizziness, drowsiness, dry mouth, constipation, stomach upset, nausea, vomiting, changes in appetite/weight, flushing, sweating, tiredness, and blurred vision may occur. Less common or rare side effects include allergic reaction, serotonin syndrome/toxicity, increased heart rate, changes in vision, muscle twitching, mental/mood changes, fever, sexual problems, numbness/tingling, shakiness, trouble urinating or dark urine, easy bruising, stomach pain, painful breasts or menstrual periods, or muscle stiffness [1054].

Desipramine: Abdominal pain, itching, confusion, dry mouth, fainting, irritability, loss of appetite, nausea, rash, restlessness, sore throat, sweating, vomiting [1055].

Doxepin: Abdominal pain, blurred vision, chest pain, chills, cold sweats, cough, dizziness, dry mouth, dry skin, headache, increased hunger or thirst, loss of appetite, nausea, nervousness, rapid weight gain, muscle spasms, restlessness, seizures, sore throat, sweating, troubled breathing, vomiting [1056].

Imipramine: Abdominal pain, blurred vision, chest pain, cough, sore throat, dizziness, dry mouth, fever, tiredness, hostility, itching, muscle spasms, nightmares, restlessness, seizures, sweating, swelling, weakness [1057].

Nortriptyline: Sedation, dry mouth, and weight gain [1052, 1053]. In addition, it can cause orthostatic hypotension, sexual dysfunction, and anticholinergic effects such as urinary retention, constipation, blurred vision, and confusion [1052].

MAOIs (including isocarboxazide, moclobemide, minaprine, phenelzine, pirlindole, selegiline, tranylcypromine, etc.): Sleep disturbances, orthostatic hypotension, sexual dysfunction, and weight gain [1048]. MAOI medications can have interactions with food high in tyramine; therefore, dietary restrictions should reduce/avoid foods with tyramine such as caffeine, chocolate, aged cheeses, aged/dried/fermented/salted/smoke/pickled/processed meats and fish, banana peels, beef/chicken liver, bouillon cubes, commercial gravies, concentrated yeast extracts, fava beans, Italian green beans, broad beans, fermented bean curd, homemade yeast-leavened bread, kimchi, orange pulp, overripe or spoiled fruits, packaged soups, red wine, sauerkraut, sherry, snow pea pods, sourdough bread, soy sauce, soybeans, soybean paste/miso, tofu, tap beer and ale, vermouth, avocados, various types of beer, eggplant, canned figs, fish roe, peanuts, port wine, raisins, raspberries, red plums, spinach, tomatoes, white wine, etc. [1058, 1059].

Moclobemide: Increased or irregular heartbeat, muscle stiffness, severe throbbing headache, slow heartbeat, or pressure in the head. Less common side effects include anxiety, vision changes, dizziness, irregular heart rate, high blood pressure, irritability, nervousness, restlessness, unusual tiredness, or weakness. Rare side effects include: aggressive behavior, bleeding gums, burning or tingling sensation, chest pain, confusion, mental changes, difficulty speaking, irregular heartbeat, feeling of something in the eye, headache, increase in urination, irregular periods, irritation or soreness of the mouth, inflammation, loss of balance, loss of interest in self, memory problems, painful urination or trouble passing stool, ringing in the ears, skin rash, stomach pain, or uncontrolled movements [1060].

Phenelzine: Dizziness, drowsiness, tiredness, weakness, problems sleeping, constipation, and dry mouth may occur. Less common or rare side effects include: fainting, mental changes, muscle stiffness, sexual problems, shaking, swollen legs, unusual weight gain, eye or vision problems, stomach pain, seizures, dark urine, yellowing eyes/skin, high blood pressure, chest pain, serotonin syndrome, or allergic reaction [1058]. Phenelzine can have interactions with food high in tyramine; therefore, dietary restrictions should reduce/avoid foods with tyramine such as caffeine, chocolate, aged cheeses, aged/dried/fermented/salted/smoke/pickled/processed meats and fish, banana peels, beef/chicken liver, bouillon cubes, commercial gravies, concentrated yeast extracts, fava beans, Italian green beans, broad beans, fermented bean curd, homemade yeast-leavened bread, kimchi, orange pulp, overripe or spoiled fruits, packaged soups, red wine, sauerkraut, sherry, snow pea pods, sourdough bread, soy sauce, soybeans, soybean paste/miso, tofu, tap beer and ale, vermouth, avocados, various types of beer, eggplant, canned figs, fish roe, peanuts, port wine, raisins, raspberries, red plums, spinach, tomatoes,

white wine, etc. [1058].

Frequency/Dose/Duration:

Per manufacturer's recommendations.

There is no clear quality evidence of superiority of one antidepressant over another. If there is a lack of efficacy of an antidepressant, it is generally preferred to switch to an alternate medication rather than increase dose, as there tends to be little incremental treatment gain while adverse effects commensurately increase [1061, 1062].

Indications for Discontinuation:

Lack of efficacy, adverse effects, non-compliance, sufficient resolution of anxiety disorder to not require medication

Rationale:

There are more than 100 moderate-quality studies, including dozens of placebo-controlled trials (see tables of evidence)—nearly all of which suggest efficacy of antidepressants for treatment of anxiety disorders (GAD, panic disorder, social anxiety disorder). The few negative trials have primarily involved MAOIs for treatment of social phobia [806, 1063] and panic disorder [810], although most placebo-controlled trials have suggested the MAOIs are effective for social phobia [946, 1022, 1023], social anxiety disorder [965], and panic disorder [964]. One trial of imipramine for treatment of panic disorder was also negative against placebo [801], and one trial of escitalopram was negative for GAD [1064].

Three trials found that combinations of CBT plus phenelzine [593], escitalopram [766], and imipramine [591] resulted in superior outcomes compared with CBT alone. Comparative trials with non-medication based treatment are relatively few, but some trials found CBT superior to imipramine [808], fluoxetine [809], and the MAOI moclobemide [806]. However, a few other trials found CBT inferior to paroxetine [656] and phenelzine [523].

One trial found venlafaxine superior to buspirone, which was in turn superior to placebo [1008].

Antidepressants have moderate adverse effects, have low to moderately cost (depending especially on duration), have quality evidence of efficacy, and are thus recommended. There are many factors affecting the selection of antidepressants.

Evidence:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Citalopram; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 322 articles in PubMed, 5991 in Scopus, 605,913 in CINAHL, 216 in Cochrane Library, 20400 in Google Scholar, and 1 from other sources†. We considered for inclusion 2 from PubMed, 2 from Scopus, 4 from CINAHL, 3 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 11 articles

considered for inclusion, 9 randomized trials and 2 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Escitalopram; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 349 articles in PubMed, 3080 in Scopus, 53 in CINAHL, 95 in Cochrane Library, 12100 in Google Scholar, and 0 from other sources†. We considered for inclusion 9 from PubMed, 4 from Scopus, 1 from CINAHL, 3 from Cochrane Library, 4 from Google Scholar, and 0 from other sources. Of the 21 articles considered for inclusion, 15 randomized studies and 5 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Fluoxetine ; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 311 articles in PubMed, 10343 in Scopus, 25 in CINAHL, 9211 in Cochrane Library, 35900 in Google Scholar, and 2 from other sources†. We considered for inclusion 4 from PubMed, 2 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 2 from other sources. Of the 8 articles considered for inclusion, 6 randomized trials and 0 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Paroxetine; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 415 articles in PubMed, 7248 in Scopus, 272 in CINAHL, 254 in Cochrane Library, 24700 in Google Scholar, and 0 from other sources†. We considered for inclusion 17 from PubMed, 2 from Scopus, 22 from CINAHL, 11 from Cochrane Library, 2 from Google Scholar, and 0 from other sources. Of the 53 articles considered for inclusion, 37 randomized trials and 10 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date

limits using the following terms: Sertraline, Zoloft; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 206 articles in PubMed, 6288 in Scopus, 136 in CINAHL, 95 in Cochrane Library, 24,600 in Google Scholar, and 0 from other sources†. We considered for inclusion 19 from PubMed, 1 from Scopus, 9 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 29 articles considered for inclusion, 17 randomized trials and 3 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Vilazodone; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 10 articles in PubMed, 221 in Scopus, 6 in CINAHL, 7 in Cochrane Library, 735 in Google Scholar, and 1 from other sources†. We considered for inclusion 4 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 6 articles considered for inclusion, 4 randomized trials and 1 systematic review met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: duloxetine hydrochloride, duloxetine, serotonin-norepinephrine reuptake inhibitor, SNRI ; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 119 articles in PubMed, 401 in Scopus, 9 in CINAHL, 26 in Cochrane Library, 3280 in Google Scholar, and 3 from other sources†. We considered for inclusion 7 from PubMed, 1 from Scopus, 2 from CINAHL, 5 from Cochrane Library, 0 from Google Scholar, and 3 from other sources. Of the 18 articles considered for inclusion, 9 randomized trials and 8 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: venlafaxine, venlafaxine extended release, serotonin-norepinephrine reuptake inhibitor, SNRI ; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized

controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 275 articles in PubMed, 4877 in Scopus, 43 in CINAHL, 130 in Cochrane Library, 18800 in Google Scholar, and 7 from other sources†. We considered for inclusion 6 from PubMed, 0 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 7 from Google Scholar, and 7 from other sources. Of the 21 articles considered for inclusion, 15 randomized trials and 5 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Amitriptyline; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 210 articles in PubMed, 4269 in Scopus, 50 in CINAHL, 129 in Cochrane Library, 18300 in Google Scholar, and 1 from other sources†. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 1 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 2 articles considered for inclusion, 1 randomized trial and 0 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Clomipramine, Clomipramine Hydrochloride, Anafranil, Hydiphen, Clomipramine Maleate; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 184 articles in PubMed, 3500 in Scopus, 3 in CINAHL, 6225 in Cochrane Library, 10200 in Google Scholar, and 10 from other sources†. We considered for inclusion 7 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 10 from other sources. Of the 17 articles considered for inclusion, 17 randomized trials and 0 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: doxepin; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 38 articles in PubMed, 671 in Scopus, 3 in

CINAHL, 25 in Cochrane Library, 5280 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 4 from PubMed, 6 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 11 articles considered for inclusion, 6 randomized trials and 4 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Imipramine; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 331 articles in PubMed, 4371 in Scopus, 133 in CINAHL, 1045 in Cochrane Library, 19500 in Google Scholar, and 4 from other sources[†]. We considered for inclusion 12 from PubMed, 2 from Scopus, 1 from CINAHL, 3 from Cochrane Library, 2 from Google Scholar, and 4 from other sources. Of the 24 articles considered for inclusion, 23 randomized trials and 1 systematic review met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Nortriptyline, anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 83 articles in PubMed, 2315 in Scopus, 14 in CINAHL, 34 in Cochrane Library, 11000 in Google Scholar, and 1 from other sources[†]. We considered for inclusion 1 from PubMed, 0 from Scopus, 0 from CINAHL, 2 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 4 articles considered for inclusion, 1 randomized trial and 1 systematic review met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: isocarboxazid; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 4 articles in PubMed, 14 in Scopus, 0 in CINAHL, 4 in Cochrane Library, 1240 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 1 article considered for

inclusion, 0 randomized trials and 1 systematic review met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Moclobemide; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 63 articles in PubMed, 1035 in Scopus, 22 in CINAHL, 35 in Cochrane Library, and 4190 in Google Scholar and 0 from other sources†. We considered for inclusion 7 from PubMed, 0 from Scopus, 0 from CINAHL, 6 from Cochrane Library, 5 from Google Scholar, and 0 from other sources. Of the 18 articles considered for inclusion, 10 randomized trials and 4 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Phenelzine, Nardil, Nardilzine: anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 73 articles in PubMed, 1687 in Scopus, 4 in CINAHL, 5 in Cochrane Library, 5830 in Google Scholar, and 2 from other sources†. We considered for inclusion 0 from PubMed, 4 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 2 from other sources. Of the 6 articles considered for inclusion, 6 randomized trials and 0 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Pirlindole; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 3 articles in PubMed, 31 in Scopus, 0 in CINAHL, 4 in Cochrane Library, 372 in Google Scholar, and 0 from other sources†. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: selegiline; anxiety, anxiety disorders,

panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 6 articles in PubMed, 836 in Scopus, 0 in CINAHL, 1 in Cochrane Library, 5310 in Google Scholar, and 0 from other sources†. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: tranylcypromine; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 8 articles in PubMed, 642 in Scopus, 3 in CINAHL, 3 in Cochrane Library, 3350 in Google Scholar, and 1 from other sources†. We considered for inclusion 1 from PubMed, 2 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 1 from other sources. Of the 5 articles considered for inclusion, 1 randomized trial and 0 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Benzodiazepines have been used for the treatment of anxiety disorders [813, 834, 835, 896, 1020, 1039, 1041, 1045, 1065-1137].

Benzodiazepines

Sometimes Recommended.

Benzodiazepines are not recommended for routine or long-term use due to risks of dependency, addiction, serious impairing adverse effects, and ensuing risks of motor vehicle crashes and other accidents. There is a high risk of patients becoming dependent on these medications, with some progressing to a substance abuse disorder. Benzodiazepines are selectively recommended for the short-term treatment of patients with anxiety disorders.

Strength of Evidence – Not Recommended, Evidence (C) – Routine use

Level of Confidence – High

Strength of Evidence – Recommended, Evidence (C) – Select use

Level of Confidence – Moderate

Indications:

Not recommended for routine use due to high potential for dependence, abuse, and other adverse effects (e.g., cognitive impairments, motor vehicle crashes and falls). Highly selective use only for those with moderate to severely affected patients with generalized anxiety disorder, social anxiety disorder, and panic disorder. May be useful for short-term use for severely affected patients with panic disorder during a time when antidepressants have been instituted and but are not yet effective. It is generally not necessary to treat phobias with benzodiazepines, and they have not been assessed in quality studies. As the adverse effects of benzodiazepines are quite considerable, the indications are more selective. Patients should generally have been provided CBT, aerobic exercise, and strengthening exercises, and failed to obtain sufficient symptoms relief despite adherence. Patients should also have generally failed to obtain sufficient symptom relief while having trialed at least three other medications that do not have the addictive properties of benzodiazepines, such as antidepressants, hydroxyzine, propranolol, and buspirone.

Benefits:

Improved anxiety symptoms

Harms:

High risk of addiction. Physical dependence and withdrawal symptoms. Considerable impairments in memory [199, 200], cognition (e.g., visuospatial ability, speed of processing, and verbal learning) [201], sedation [201], and risk of motor vehicle crashes [202, 203], dementia [204, 1138], and falls [205, 206].

Sedative properties have consistent epidemiological evidence of considerably increased motor vehicle crash risks to thus be significantly problematic if not precluded for safety-critical workers. Adverse effects also include drowsiness, fatigue, confusion, slurred speech, lightheadedness, and blurred vision. One trial reported increased aggression due to alprazolam [1083].

Frequency/Dose/Duration:

Multiple different benzodiazepines and dose regimens have been used, with no consistent quality evidence of superiority of one benzodiazepine over another. Doses in trials have often included

gradually increased dosage while initiating treatment. Dosing regimens in the RCTs have included the following:

Alprazolam 1-2 mg up to QID [1139]

Alprazolam 2 mg QD [1065, 1066]

Alprazolam 1.5-3 mg/day [1140]

Alprazolam 0.5-4.5 mg/day [1070]

Clonazepam 0.125-0.25 mg/day [1123]

Clonazepam 0.5-2 mg/day [982]

Clonazepam 0.5 mg TID [1121]

Clonazepam 0.5-3 mg/day [1120]

Clorazepate 15 mg QHS [1094]

Chlorazepate 22.5-45 mg/day [1096]

Chlordiazepoxide 10-30 mg/day [1113, 1114]

Chlordiazepoxide 50-100 mg/day for severe anxiety [1119]

Diazepam 15 mg/day [1125]

Diazepam 15-30 mg/day [1117]

Diazepam 10-45 mg/day [1118]

Lorazepam 2-4 mg/day [1100]

Lorazepam 3 mg BID [1101]

Lorazepam 4-6 mg/day [1102]

Oxazepam 30 mg/day [1088]

Oxazepam 15-90 mg/day [1089]

Indications for Discontinuation:

Intolerability, adverse effects, non-compliance, lack of efficacy, gaining employment in a safety-critical work position. (See also [Benzodiazepine Discontinuation and Tapering.](#))

Rationale:

There are numerous moderate-quality placebo-controlled RCTs evaluating benzodiazepines (nearly all of which involve alprazolam, clonazepam, clorazepate, diazepam, lorazepam, and chlordiazepoxide). Symptom improvement has been demonstrated consistently across the studies [835, 896, 1020, 1041, 1066, 1070-1073, 1081-1083, 1088, 1095, 1096, 1100-1104, 1108, 1109, 1114, 1115, 1117, 1118, 1120, 1121, 1123-1125, 1127, 1141, 1142]. Nearly all quality studies assessed efficacy for treatment of GAD or panic disorder, with a few assessing social anxiety disorder. One of the studies of panic disorder assessed patients with panic disorder with agoraphobia [896]. One trial reported reduced anxiety symptoms with alprazolam, but aggression was increased [1083].

Regarding comparative trials, there is no clear pattern of superiority of benzodiazepines. One trial showed comparable efficacy of propranolol to alprazolam for treatment of agoraphobia [1143], while another suggested superiority of alprazolam for treatment of panic attacks [1144]. One trial suggested imipramine was superior for dysphoria and negative thinking, while alprazolam was superior for somatic symptoms [1067]. One trial suggested more adverse effects with diazepam compared with alprazolam [1070]. One crossover trial reported imipramine was superior to chlordiazepoxide, which was superior to placebo [1114]. One crossover trial reported chlorpromazine was comparable to chlordiazepoxide [1119]. One reported superiority of chlordiazepoxide to paroxetine [1124], while another suggested equivalency between chlordiazepoxide and

propranolol [1145]. A combination of paroxetine with clonazepam was superior to paroxetine alone [1124]. Two trials suggest comparable efficacy of alprazolam to pregabalin [968, 1146] and one trial suggested superiority of pregabalin to alprazolam [1147].

Benzodiazepines have moderate adverse effects (including addiction potential), are low to moderate cost (depending upon duration of treatment), and have quality evidence of efficacy for treatment of anxiety disorders; therefore, they are selectively recommended. Patients should have generally been treated, complied with, and obtained insufficient symptom relief with CBT, aerobic exercise, strengthening exercise, and at least 2 nonaddictive medication trials (e.g., antidepressants, propranolol, hydroxyzine, buspirone). This recommendation was reduced from “B” level evidence to “C” level evidence due to the degree of adverse effects.

Evidence:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Alprazolam; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 246 articles in PubMed, 5431 in Scopus, 12 in CINAHL, 274 in Cochrane Library, 10,400 in Google Scholar, and 0 from other sources†. We considered for inclusion 22 from PubMed, 15 from Scopus, 1 from CINAHL, 5 from Cochrane Library, 3 from Google Scholar, and 0 from other sources. Of the 46 articles considered for inclusion, 36 randomized trials and 2 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Chlordiazepoxide; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 126 articles in PubMed, 1978 in Scopus, 0 in CINAHL, 132 in Cochrane Library, 4710 in Google Scholar, and 0 from other sources†. We considered for inclusion 7 from PubMed, 2 from Scopus, 0 from CINAHL, 2 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 11 articles considered for inclusion, 6 randomized trials and 2 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Clonazepam; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*,

randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 67 articles in PubMed, 2802 in Scopus, 7 in CINAHL, 40 in Cochrane Library, 9560 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 16 from PubMed, 5 from Scopus, 2 from CINAHL, 1 from Cochrane Library, 5 from Google Scholar, and 0 from other sources. Of the 27 articles considered for inclusion, 18 randomized trials and 1 systematic review met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Clorazepate, Clorazepate Dipotassium; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 24 articles in PubMed, 691 in Scopus, 17 in CINAHL, 33 in Cochrane Library, 1,450 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 5 from PubMed, 6 from Scopus, 0 from CINAHL, 5 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 17 articles considered for inclusion, 10 randomized trials and 2 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Diazepam; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 627 articles in PubMed, 3760 in Scopus, 244 in CINAHL, 19 in Cochrane Library, 17,400 in Google Scholar, and 2 from other sources[†]. We considered for inclusion 12 from PubMed, 2 from Scopus, 6 from CINAHL, 1 from Cochrane Library, 0 from Google Scholar, and 2 from other sources. Of the 23 articles considered for inclusion, 14 randomized trials and 2 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: lorazepam; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 149 articles in PubMed, 3,393 in Scopus, 84 in CINAHL, 143 in Cochrane Library, 11,900 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 15 from PubMed, 4 from

Scopus, 2 from CINAHL, 5 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 27 articles considered for inclusion, 24 randomized trials and 1 systematic review met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Oxazepam; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 46 articles in PubMed, 1120 in Scopus, 6 in CINAHL, 51 in Cochrane Library, 3750 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 3 from PubMed, 2 from Scopus, 2 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 0 from other sources. Of the 9 articles considered for inclusion, 4 randomized trials and 0 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Temazepam; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 18 articles in PubMed, 882 in Scopus, 0 in CINAHL, 21 in Cochrane Library, 3260 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 2 from PubMed, 2 from Scopus, 0 articles met the inclusion criteria from CINAHL, 0 articles met the inclusion criteria from Cochrane Library, 0 articles met the inclusion criteria from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

[†] The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Buspirone has been used in the treatment of anxiety disorders [802, 1008, 1028, 1029, 1130-1134, 1136, 1137, 1148-1157].

Buspirone

Recommended.

Buspirone is recommended for the treatment of patients with anxiety disorders, especially generalized anxiety disorder.

Strength of Evidence – Recommended, Evidence (C)

Level of Confidence – Low

<i>Indications:</i>	Anxiety disorders, especially GAD (for which there is the most consistent evidence of efficacy)
<i>Benefits:</i>	Reduced anxiety symptoms
<i>Harms:</i>	Drowsiness, dizziness, chest pain, confusion, palpitations, incoordination, weakness, fatigue, nervousness, restlessness.
<i>Frequency/Dose/Duration:</i>	Most studies used gradually increasing daily dose regimens that varied, such as buspirone 5 mg increasing to 40 mg/day [1151, 1152]. Others used 5 mg BID that was increased to 5 mg QID [1155], while others increased up to 10 mg TID.
<i>Indications for Discontinuation:</i>	Intolerability, adverse effects, non-compliance, lack of efficacy.
<i>Rationale:</i>	Multiple moderate-quality, placebo-controlled studies mostly suggest efficacy of buspirone for GAD [1134, 1137, 1151, 1152, 1155], although some studies are statistically negative [1028, 1157], especially for social phobia [1156] and panic disorder [1029]. One trial suggested inferiority to hydroxyzine [1149]. One trial suggested superiority of buspirone plus CBT compared with placebo for panic disorder with agoraphobia [802]. Studies generally suggest equivalency to, but better tolerability compared with, benzodiazepines [1137, 1151, 1155]. Buspirone is not invasive, has low adverse effects, is low cost and thus is recommended, especially for treatment of GAD. There is unclear evidence for other anxiety disorders.
<i>Evidence:</i>	A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: buspirone; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 137 articles in PubMed, 2510 in Scopus, 13 in CINAHL, 99 in Cochrane Library, 8860 in Google Scholar, and 2 from other sources†. We considered for inclusion 31 from PubMed, 17 from Scopus, 0 from CINAHL, 5 from Cochrane Library, 3 from Google Scholar, and 8 from other sources. Of the 64 articles considered for inclusion, 26 randomized trials and 5 systematic reviews met the inclusion criteria.

Quetiapine has been used for treatment of anxiety disorders [938, 939, 1158-1164].

Antipsychotics (Quetiapine)

Recommended.

Quetiapine is moderately recommended for the treatment of patients with anxiety disorders.

Strength of Evidence – Moderately Recommended, Evidence (B)

Level of Confidence – Moderate

<i>Indications:</i>	Anxiety disorders, particularly GAD (for which there is consistent evidence of efficacy). Other medications should generally be trialed first, such as SSRIs, SNRIs, and buspirone.
<i>Benefits:</i>	Improvements in anxiety symptoms, sleep, and function
<i>Harms:</i>	Dizziness, faintness, lightheadedness, drowsiness, chills, sleepiness, drowsiness, fatigue, diarrhea, constipation, blurred vision, dry mouth.
<i>Frequency/Dose/Duration:</i>	There are multiple dosing regimens in the quality literature; doses used in the higher quality trials are listed below. Quetiapine dosing regimens used generally ranged from 50 to 300 mg/day [1158], while others used increasing dose regimens such as an initial XR dose of 50 mg/day then increased to 150 mg on day 3 and 300mg/day at weeks 3-4 among some patients [1159].
<i>Indications for Discontinuation:</i>	Intolerability, adverse effects, non-compliance, lack of efficacy
<i>Rationale:</i>	Many moderate-quality placebo-controlled trials have suggested efficacy of quetiapine for treatment of GAD [938, 939, 1159, 1161, 1165]. Trials have suggested lack of additive benefit of quetiapine in addition to paroxetine [1160], equivalency to escitalopram [938], and equivalency to paroxetine [939]. Quetiapine has low to moderate adverse effects (which include metabolic concerns), is low to moderate cost, and has consistent evidence of efficacy; thus, it is recommended for treatment of GAD. Other first-line agents are recommended to be trialed first, such as SSRIs, SNRIs, and buspirone.
<i>Evidence:</i>	A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Aripiprazole; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 111 articles in PubMed, 1976 in Scopus, 12 in CINAHL, 2 in Cochrane Library, 8380 in Google Scholar, and 0 from other sources†. We considered for inclusion 3 from PubMed, 0 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 4 from Google Scholar, and 0 from other sources. Of the 8 articles considered for inclusion, 0 randomized trials and 4 systematic reviews met the inclusion criteria. A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Bupropion; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled

clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 124 articles in PubMed, 798 in Scopus, 45 in CINAHL, 0 in Cochrane Library, 14400 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 1 from PubMed, 0 from Scopus, 3 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 0 from other sources. Of the 6 articles considered for inclusion, 1 randomized trial and 1 systematic review met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Quetiapine Fumarate, Quetiapine; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 114 articles in PubMed, 2,955 in Scopus, 9 in CINAHL, 64 in Cochrane Library, 13,100 in Google Scholar, and 3 from other sources[†]. We considered for inclusion 11 from PubMed, 5 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 4 from Google Scholar, and 3 from other sources. Of the 23 articles considered for inclusion, 10 randomized trials and 7 systematic reviews met the inclusion criteria.

[†] The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens, then the remaining articles are not reviewed due to a lack of relevancy.

Beta blockers, especially propranolol and atenolol, have been used for the treatment of anxiety disorders [937, 1143-1145, 1166-1173].

Adrenergic Inhibitors – Beta-blockers

Moderately Recommended.

Propranolol and atenolol are moderately recommended for the treatment of anxiety disorders. They are often used for physical symptoms of anxiety, such as increased heart rate and for situations in which reducing the physical symptoms could be beneficial, such as in a public speaking situation.

Strength of Evidence – Moderately Recommended, Evidence (B)

Level of Confidence – Moderate

<i>Indications:</i>	Generalized anxiety and other anxiety disorders. Generally should have had treatment with CBT, aerobic exercise, and strengthening exercises. May be used in combination.
<i>Benefits:</i>	Improved anxiety symptoms. Antihypertensive properties may be used for an advantage, although those properties also produce some of the adverse effects.
<i>Harms:</i>	Drowsiness, slow heart rate, syncope, heart block, diarrhea, dry eyes, weakness, tiredness, rash, sleeping disturbance, muscle cramps, swollen ankles
<i>Frequency/Dose/Duration:</i>	Propranolol 40 mg QID [1166]
<i>Indications for Discontinuation:</i>	Resolution of anxiety symptoms, adverse effects, non-compliance
<i>Rationale:</i>	All moderate-quality placebo-controlled trials have suggested efficacy of propranolol for treatment of anxiety [1144, 1145, 1166], including a randomized crossover trial showing efficacy [1166]. One trial showed comparable efficacy with alprazolam for treatment of agoraphobia [1143], while another suggested superiority of alprazolam for treatment of panic attacks [1144]. Propranolol is often used for physical symptoms of anxiety, such as increased heart rate. Propranolol (and also atenolol) are used for situations in which reducing the physical symptoms could be beneficial, such as in a public speaking situation. Beta-blockers can reduce the physical sensation of anxiety without the downside of other as-needed medications that may impair cognition (e.g., benzodiazepines). Propranolol is typically non-invasive, has low to moderate adverse effects, is low to moderate cost (depending upon treatment duration), and has evidence of efficacy for the treatment of anxiety; thus, it is recommended.
<i>Evidence:</i>	A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Propranolol; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 98 articles in PubMed, 356 in Scopus, 4 in CINAHL, 77 in Cochrane Library, 9240 in Google Scholar, and 3 from other sources†. We considered for inclusion 5 from PubMed, 0 from

Scopus, 1 from CINAHL, 2 from Cochrane Library, 0 from Google Scholar, and 6 from other sources. Of the 14 articles considered for inclusion, 9 randomized trials and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens, then the remaining articles are not reviewed due to a lack of relevancy.

Evidence:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Atenolol; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 26 articles in PubMed, 806 in Scopus, 0 in CINAHL, 18 in Cochrane Library, 3710 in Google Scholar, and 3 from other sources†. We considered for inclusion 2 from PubMed, 4 from Scopus, 0 from CINAHL, 1 from Cochrane Library, 0 from Google Scholar, and 3 from other sources. Of the 10 articles considered for inclusion, 4 randomized trials and 0 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Gabapentin is an antiepileptic that has been used to treat perioperative anxiety [1174-1179].

Gabapentin

No Recommendation.

There is no recommendation for or against gabapentin for the treatment of patients with anxiety disorders.

Strength of Evidence – No Recommendation, Insufficient Evidence (I)

Level of Confidence – Low

Rationale:

There are few quality trials, which substantially conflict. One placebo-controlled trial for treatment of panic disorder suggested no differences, although post-hoc analyses suggested improvements in the more severely affected female patients [1179]. A second moderate-quality trial for treatment of preoperative catastrophizing patients suggested efficacy [1174]. One trial of single-dose gabapentin for preoperative anxiety suggested superiority to hydroxyzine and placebo [1180]. Gabapentin is an analog to pregabalin, which has evidence of efficacy. However, the evidence for gabapentin alone is not robust for the treatment of anxiety disorders other than perioperative; thus, there is no recommendation for the use of gabapentin for the treatment of anxiety disorders. (See perioperative guidance elsewhere, particularly in the [Low Back Disorders](#) and [Hip and Groin Disorders](#) guidelines.)

Evidence:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: gabapentin; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 97 articles in PubMed, 3,598 in Scopus, 28 in CINAHL, 15 in Cochrane Library, 13,100 in Google Scholar, and 1 from other sources[†]. We considered for inclusion 8 from PubMed, 1 from Scopus, 0 from CINAHL, 2 from Cochrane Library, 2 from Google Scholar, and 1 from other sources. Of the 14 articles considered for inclusion, 3 randomized trials and 5 systematic reviews met the inclusion criteria.

[†] The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Pregabalin has been used for the treatment of patients with anxiety disorders [1015, 1146, 1147, 1181-1185].

Pregabalin

Moderately Recommended.

Pregabalin is moderately recommended for the treatment of patients with anxiety disorders.

Strength of Evidence – Moderately Recommended, Evidence (B)

Level of Confidence – Moderate

<i>Indications:</i>	Generalized anxiety and other anxiety disorders. Generally should have had treatment with CBT, aerobic exercise, and strengthening exercises. May be used in combination. Has been used preoperatively and perioperatively.
<i>Benefits:</i>	Improved anxiety symptoms with relatively early onset of action. Few rebound anxiety problems after discontinuation [1182].
<i>Harms:</i>	Ataxia, blurred vision, constipation, diplopia, dizziness, drowsiness, fatigue, headache, peripheral edema, tremor, weight gain, visual field loss, accidental injury, xerostomia, and infection. Abnormal gait, abnormality in thinking, amnesia, arthralgia, asthenia, cognitive dysfunction, confusion, edema, neuropathy, sinusitis, speech disturbance, vertigo, visual disturbance, myasthenia, amblyopia, increased appetite, and twitching. See below for a comprehensive list of adverse effects.
<i>Frequency/Dose/Duration:</i>	Pregabalin 400 mg/day is effective and has less adverse effects compared with pregabalin 600 mg/day [1015]
<i>Indications for Discontinuation:</i>	Resolution of anxiety symptoms, adverse effects, non-compliance
<i>Rationale:</i>	There are multiple moderate quality placebo-controlled trials of pregabalin for treatment of GAD and all studies suggest efficacy. Pregabalin is not invasive, has low to moderate adverse effects, and has consistent evidence of efficacy for treatment of anxiety disorders; thus, it is moderately recommended for treatment of anxiety disorders.
<i>Evidence:</i>	A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Pregabalin; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 328 articles in PubMed, 7531 in Scopus, 112 in CINAHL, 23 in Cochrane Library, 8020 in Google Scholar, and 1 from other sources†. We considered for inclusion 19 from PubMed, 0 from Scopus, 6 from CINAHL, 1 from Cochrane Library, 17 from Google Scholar, and 1 from other sources. Of the 44 articles considered for inclusion, 9 randomized trials and 12 systematic reviews met the inclusion criteria.

Valproic acid has been used for treatment of anxiety disorders [1186].

Valproic Acid and Valproate

No Recommendation.

There is no recommendation regarding use of valproic acid for treatment of anxiety disorders.

Strength of Evidence – No Recommendation, Insufficient Evidence (I)

Level of Confidence – Low

Rationale:

There is one moderate-quality placebo-controlled trial for treatment of GAD, with limited self-reported data that suggested potential efficacy [1186]. Absent more detailed information and additional publications on the efficacy of valproic acid, there is no recommendation.

Evidence:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Valproate, Valproic acid; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 112 articles in PubMed, 2,606 in Scopus, 30 in CINAHL, 540 in Cochrane Library, 10,900 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 3 from PubMed, 0 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 4 articles considered for inclusion, 1 randomized trial and 0 systematic reviews met the inclusion criteria.

[†] The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens, then the remaining articles are not reviewed due to a lack of relevancy.

Hydroxyzine has been used for treatment of anxiety disorders [1180, 1187-1189].

Antihistamine (Hydroxyzine)

Recommended.

Hydroxyzine is recommended for the treatment of patients with anxiety disorders.

Strength of Evidence – Recommended, Evidence (C)

Level of Confidence – Low

<i>Indications:</i>	Generalized anxiety disorder. May be used as a non-addicting alternative to benzodiazepines, often for breakthrough symptoms in addition to CBT and SSRI/SNRI treatment. Generally should have had prior treatment with CBT, aerobic exercise, and strengthening exercises. Hydroxyzine may be of particular use for primarily nocturnal symptoms to take advantage of its sedating properties, provided the daytime somnolence is not excessive. Other medications are generally preferred. Gabapentin is generally preferable for pre/perioperative use.
<i>Benefits:</i>	Reduces anxiety symptoms and causes sedative effects, which may be selectively beneficial
<i>Harms:</i>	Sedative effects. Paradoxical increased anxiety. Generally not indicated for patients with safety-critical work.
<i>Frequency/Dose/Duration:</i>	Hydroxyzine 12.5 mg every morning, 12.5 mg at noon, and 50 mg at bedtime.
<i>Indications for Discontinuation:</i>	Resolution of anxiety symptoms, intolerance, non-compliance, excessive adverse effects.
<i>Rationale:</i>	Two moderate-quality trials found hydroxyzine was superior to placebo for treatment of generalized anxiety disorder [1187]. One trial evaluated hydroxyzine as a single-dose preoperative treatment and found gabapentin was superior [1180]. Hydroxyzine is not invasive, has sedative effects, and is low cost; thus, it is selectively recommended for treatment of anxiety disorders, especially where there is a need for sedative effects (e.g., insomnia).
<i>Evidence:</i>	A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Hydroxyzine; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 33 articles in PubMed, 555 in Scopus, 3 in CINAHL, 38 in Cochrane Library, 2080 in Google Scholar, and 0 from other sources†. We considered for inclusion 4 from PubMed, 4 from Scopus, 0 from CINAHL, 1 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 9 articles considered for inclusion, 4 randomized trials and 2 systematic reviews met the inclusion criteria.

Alternative Methods

Nutraceuticals has been used to treat anxiety [1218-1230].

Nutraceuticals

No Recommendation.

There is no recommendation for or against the use of nutraceuticals in the treatment of patients with anxiety disorders. (See also separate recommendations regarding valerian, lavender oil, kava, and St. John's wort.)

Strength of Evidence – No Recommendation, Insufficient Evidence (I)

Level of Confidence – Low

Rationale:

Valerian, lavender oil, kava, and St. John's wort are addressed in separate recommendations. There are no quality trials of other nutraceuticals for treatment of anxiety disorders. Thus, there is no recommendation for other nutraceuticals.

Evidence:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: nutraceuticals and dietary supplements; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 174 articles in PubMed, 71 in Scopus, 83 in CINAHL, 54 in Cochrane Library, 2390 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 6 from PubMed, 0 from Scopus, 2 from CINAHL, 1 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 11 articles considered for inclusion, 4 randomized trials and 4 systematic reviews met the inclusion criteria.

[†] The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

St. John's Wort, a non-FDA approved dietary supplement, has been used to treat anxiety [1231].

St. John's Wort (*Hypericum Perforatum*)

Not Recommended.

St. John's wort (*Hypericum Perforatum*) is not recommended for the treatment of patients with anxiety disorders.

Strength of Evidence – Not Recommended, Evidence (C)

Level of Confidence – Low

Rationale:

There is one moderate-quality placebo-controlled trial, which found a lack of efficacy of St. John's wort for treatment of social phobia [1231]; thus, it is not recommended.

Evidence:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: St John's Wort; Hypericum, hypericum perforatum, anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 53 articles in PubMed, 1,484 in Scopus, 25 in CINAHL, 0 in Cochrane Library, 3,620 in Google Scholar, and 1 from other sources[†]. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 1 article considered for inclusion, 1 randomized trial and 0 systematic studies met the inclusion criteria.

[†] The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens, then the remaining articles are not reviewed due to a lack of relevancy.

Kava extract has been used to treat anxiety [1088, 1148, 1220, 1232-1254].

Kava Extract

No Recommendation.

There is no recommendation for or against the use of kava extract in the treatment of patients with anxiety disorders.

Strength of Evidence – No Recommendation, Insufficient Evidence (I)

Level of Confidence – Low

Rationale:

There are many placebo-controlled trials of kava, and the results materially conflict with multiple positive and negative studies. For example, of the 5 quality studies with at least 100 participants, 3 studies suggested lack of efficacy and 2 studies suggested efficacy. Thus, there is no recommendation regarding kava.

Evidence:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Kava Extract; kava, anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 51 articles in PubMed, 894 in Scopus, 40 in CINAHL, 29 in Cochrane Library, 1940 in Google Scholar, and 2 from other sources[†]. We considered for inclusion 15 from PubMed, 2 from Scopus, 5 from CINAHL, 1 from Cochrane Library, 3 from Google Scholar, and 2 from other sources. Of the 28 articles considered for inclusion, 16 randomized trials and 12 systematic studies met the inclusion criteria.

[†] The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Lavender oil has been used to treat anxiety [1204, 1257-1264].

Lavender Oil

No Recommendation.

There is no recommendation for or against the use of lavender oil in the treatment of patients with anxiety disorders.

Strength of Evidence – No Recommendation, Insufficient Evidence (I)

Level of Confidence – Low

Rationale:

There are 2 moderate-quality trials of lavender oil by the same research group that attempted to blind the participants; however, the publications do not report blinding success [1257, 1258] and unblinding by using 1/1000 the amount of lavender for the placebo groups appears likely. Another study reported comparable (in)efficacy to lorazepam and higher adverse effects in the lorazepam group [1204], but likely was at least partially unblinded. Both reports suggest efficacy. Lavender oil needs to be evaluated against placebo while addressing the research methods weakness without conflicts of interest to provide an evidence-based recommendation.

Evidence:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Lavender Oil, Silexan; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 36 articles in PubMed, 210 in Scopus, 44 in CINAHL, 19 in Cochrane Library, 1,890 in Google Scholar, and 3 from other sources[†]. We considered for inclusion 2 from PubMed, 4 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 3 from other sources. Of the 9 articles considered for inclusion, 3 randomized trials and 5 systematic reviews met the inclusion criteria.

[†] The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Valerian has been used to treat anxiety [1266-1271].

Valerian

Not Recommended.

Valerian is not recommended for the treatment of patients with anxiety disorders.

Strength of Evidence – Not Recommended, Evidence (C)

Level of Confidence – Low

Rationale:

One quality trial suggested valerian was not superior to placebo; thus, valerian is not recommended for the treatment of anxiety disorders [1242].

Evidence:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Valerian; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 22 articles in PubMed, 424 in Scopus, 14 in CINAHL, 10 in Cochrane Library, 2,190 in Google Scholar, and 2 from other sources[†]. We considered for inclusion 0 from PubMed, 5 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 2 from other sources. Of the 8 articles considered for inclusion, 2 randomized trials and 2 systematic reviews met the inclusion criteria.

[†] The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Marijuana has been used to treat anxiety [1272-1289].

Marijuana, Cannabis, Cannabinoids, and Cannabidiol
Not Recommended.

The use of marijuana, cannabis, cannabinoids, and cannabidiol is not recommended for the treatment of patients with anxiety disorders.

Strength of Evidence – Not Recommended, Insufficient Evidence (I)

Level of Confidence – Low

Rationale:

There are no quality trials of cannabinoids for ongoing treatment of anxiety disorders. Cannabinoids have significant adverse effects and are addictive; thus, in the absence of evidence of efficacy, they are not recommended.

Evidence:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Marijuana, Medical Marijuana, Cannabis, Cannabinoids, Cannabidiol; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 95 articles in PubMed, 1,949 in Scopus, 70 in CINAHL, 27 in Cochrane Library, 1,080 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 11 from PubMed, 2 from Scopus, 2 from CINAHL, 0 from Cochrane Library, 3 from Google Scholar, and 0 from other sources. Of the 18 articles considered for inclusion, 1 randomized trial and 12 systematic reviews met the inclusion criteria.

[†] The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Neuromodulation Therapies

Transcranial magnetic stimulation and repetitive transcranial magnetic stimulation have been used to treat anxiety [1290-1299].

Transcranial Magnetic Stimulation and Repetitive Transcranial Magnetic Stimulation (rTMS) No Recommendation.

There is no recommendation for or against transcranial magnetic stimulation and repetitive transcranial magnetic stimulation (rTMS) for patients with anxiety disorders.

Strength of Evidence – No Recommendation, Insufficient Evidence (I)

Level of Confidence – Low

Rationale:

There are four quality sham-controlled trials, which conflict regarding whether rTMS is effective [1290, 1300]; thus, there is no recommendation for or against rTMS for treatment of anxiety disorders.

Evidence:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Transcranial Magnetic Stimulation; repetitive transcranial magnetic stimulation, tms, rtms, anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 198 articles in PubMed, 6,262 in Scopus, 51 in CINAHL, 1,294 in Cochrane Library, 10,100 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 10 from PubMed, 0 from Scopus, 2 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 11 articles considered for inclusion, 5 randomized trials and 4 systematic reviews met the inclusion criteria.

[†] The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Brainwave synchronization is a type of neuromodulation [1301-1305].

Brainwave Synchronization

No Recommendation.

There is no recommendation for or against the use of brainwave synchronization in the treatment of patients with anxiety disorders.

Strength of Evidence – No Recommendation, Insufficient Evidence (I)

Level of Confidence – Low

Rationale:

There is no quality evidence for brainwave synchronization; thus, there is no recommendation.

Evidence:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Brain Wave Synchronizers, Brain Wave Entrainment; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 4 articles in PubMed, 34 in Scopus, 0 in CINAHL, 1 in Cochrane Library, 4,120 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 3 from PubMed, 2 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

[†] The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Allied Health Interventions

Acupressure is an alternative medicine technique during which physical pressure is applied to acupuncture points on the body located along meridians or acupoints [1306-1311].

Acupressure

No Recommendation.

There is no recommendation for or against acupressure for the treatment of anxiety disorders.

Strength of Evidence – No Recommendation, Insufficient Evidence (I)

Level of Confidence – Low

Rationale:

There are no quality trials of acupressure for treatment of anxiety disorders; thus, there is no recommendation.

Evidence:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Acupressure; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 48 articles in PubMed, 506 in Scopus, 48 in CINAHL, 18 in Cochrane Library, 2,860 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 2 from PubMed, 3 from Scopus, 1 from CINAHL, 1 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 7 articles considered for inclusion, 0 randomized trials and 2 systematic studies met the inclusion criteria.

[†]The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Acupuncture has been used to treat anxiety [1312-1332].

Acupuncture
Not Recommended.

Acupuncture is not recommended to treat anxiety disorders.

Strength of Evidence – Not Recommended, Evidence (C)

Level of Confidence – Low

Rationale:

There is one sham-controlled trial of acupuncture to treat generalized anxiety disorder and found lack of efficacy [1332]. A substantially lower-quality trial with a wait-control bias suggested potential efficacy. Acupuncture is minimally invasive, has low adverse effects, is cumulatively moderate to high cost, but with sham-controlled evidence of a lack of efficacy is not recommended.

Evidence:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Acupuncture; acupuncture therapy, anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 298 articles in PubMed, 647 in Scopus, 312 in CINAHL, 168 in Cochrane Library, 15,400 in Google Scholar, and 4 from other sources†. We considered for inclusion 8 from PubMed, 4 from Scopus, 2 from CINAHL, 3 from Cochrane Library, 0 from Google Scholar, and 4 from other sources. Of the 21 articles considered for inclusion, 3 randomized trials and 3 systematic reviews met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens, then the remaining articles are not reviewed due to a lack of relevancy.

Massage therapy has been used for the treatment of anxiety [1333-1339].

Massage

No Recommendation.

There is no recommendation for or against massage for the treatment of anxiety disorders.

Strength of Evidence – No Recommendation, Insufficient Evidence (I)

Level of Confidence – Low

Rationale:

There are two quality studies of the use of massage for anxiety disorders; the higher-quality study found a lack of efficacy, whereas the lower-quality suggested efficacy. The studies conflict; thus, there is no recommendation regarding use of massage for treatment of anxiety disorders.

Evidence:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Massage; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 262 articles in PubMed, 1,584 in Scopus, 334 in CINAHL, 106 in Cochrane Library, 14,400 in Google Scholar, and 0 from other sources†. We considered for inclusion 2 from PubMed, 2 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 1 from other sources. Of the 7 articles considered for inclusion, 2 randomized trials and 1 systematic review met the inclusion criteria.

† The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Therapeutic touch has been used for the treatment of anxiety [1340-1343].

Therapeutic Touch

No Recommendation.

There is no recommendation for or against therapeutic touch for the treatment of anxiety disorders.

Strength of Evidence – No Recommendation, Insufficient Evidence (I)

Level of Confidence – Low

Rationale:

There are no quality studies regarding the use of massage for anxiety disorders; thus, there is no recommendation.

Evidence:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Therapeutic Touch ; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 656 articles in PubMed, 1,484 in Scopus, 59 in CINAHL, 27 in Cochrane Library, 13,500 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 3 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 3 articles considered for inclusion, 0 randomized trials and 3 systematic reviews met the inclusion criteria.

[†] The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens, then the remaining articles are not reviewed due to a lack of relevancy.

Physical medicine treatment has been used for the treatment of anxiety [1344, 1345].

Physical Medicine Treatment

No Recommendation.

There is no recommendation for or against physical medicine treatment for the treatment of anxiety disorders.

Strength of Evidence – No Recommendation, Insufficient Evidence (I)

Level of Confidence – Low

Evidence:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: physical medicine, physical medicine treatment, physical medicine treatment and rehabilitation; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 1606 articles in PubMed, 768 in Scopus, 10 in CINAHL, 51 in Cochrane Library, 25000 in Google Scholar, and 0 from other sources[†]. We considered for inclusion 1 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 1 randomized trial and 0 systematic reviews met the inclusion criteria.

[†] The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Benzodiazepine Discontinuation and Tapering

Benzodiazepines are among the drugs most commonly associated with overdoses and deaths, with 11,537 annual deaths in 2017 associated with benzodiazepines [1346]. Benzodiazepines are one of the most misused/abused medications, with an estimated prevalence of 2.3% [1347]. The adverse effects of benzodiazepines are considerable and the need to taper and discontinue benzodiazepines is relatively common. Benzodiazepines may cause dependence within 4-6 weeks of continuous treatment [1142, 1348-1352] and are associated with withdrawal symptoms that appear to be related to dose, duration of treatment, and speed of taper [1209, 1215, 1348, 1351]. Although most cases with withdrawal symptoms in RCTs are mild [1209, 1348, 1351], withdrawal symptoms can be severe, life-threatening, and may be associated with death [1352-1354].

Benzodiazepine Discontinuation and Tapering

Recommended.

Benzodiazepine discontinuation and tapering are recommended in the treatment of anxiety disorders.

Strength of Evidence – **Recommended, Evidence (C)**

Level of Confidence – **Moderate**

Indications:

Patients treated for and having had a resolved acute anxiety disorder and who are benzodiazepine-naïve should generally require no tapering. Patients with an acute anxiety disorder and treated with continuous benzodiazepines for longer than 2-3 weeks duration may benefit from brief tapering over 3 to 7 days. Longer tapers are generally advised for those using benzodiazepines over longer periods of time. Discontinuation of benzodiazepines is recommended for patients who co-use opioids (see [Opioids guideline](#), including Tapering), have not realized significant functional benefits, underwent rapid dose escalation without benefit, have deteriorating function despite increasing dose, have misrepresentations regarding prescription loss/theft/early refill requests, have involvement with law enforcement, are actively addicted to another substance(s), have diversion, have sustained significant adverse effects, and/or lack symptoms and have reasons to suspect that there is no ongoing need for the benzodiazepine [1355].

Discontinuation is also recommended for subacute and chronic anxiety disorder patients who: i) used benzodiazepines on a chronic basis, and ii) have any one of the following: no demonstrated anxiety relief, noncompliance, aberrant drug screening results (especially with other CNS depressants and/or diversion), adverse effects (e.g., cognitive impairment, falls, poor judgment, untreated sleep apnea, and concurrent use of depressant medications such as opioids and diphenhydramine) [1356, 1357]. Tapering is especially recommended if the benzodiazepine was used at a moderate or high level on a chronic basis.

Consultation with an addiction specialist or psychiatrist is recommended for complex patients (e.g., high-dose patients, prior withdrawal problems, complex psychosocial confounders, complicating medical conditions). Transitioning to

CBT, aerobic exercise, strengthening exercise, an antidepressant, hydroxyzine, pregabalin, propranolol, quetiapine, and/or buspirone is generally indicated to assist with tapering and symptom management [1196, 1358-1364], although a Cochrane review found the overall quality of evidence to be low [1365]. Odansetron and electroacupuncture have been shown to be ineffective [1366].

Frequency/Duration:

The duration of a taper is empirical, dependent on dose, prior benzodiazepine use duration, and informed patient decision-making. Rates of the taper vary, and there is no quality head-to-head evidence regarding rates of taper. Accordingly, the speed of the taper should generally include an informed choice involving the patient, as some will prefer a faster or slower taper, although evidence suggests slower tapers are generally more successful [1367].

The following are options:

- Reductions of ~5–10% per week [1367]
- Reductions in dose of 10% per week [1368]
- Reductions of 12.5–25% per week based on withdrawal symptoms [1358]
- Reductions in dose of 25% per week [1369]
- Clonazepam tapering at a rate of 0.25 mg per 2 weeks (e.g., 1.0 mg/day tapered over 6 weeks, 1.5 mg/day tapered over 10 weeks, 2.0 mg/day tapered over 14 weeks, and 2.5 mg/day tapered over 18 weeks) [1209]

Dose may be converted to a diazepam dose equivalent [1355].

As CBT has been found to increase the success of tapering, it should generally be added to all tapering regimens [1358].

The following process has been recommended [656]:

1. Develop a taper plan. Elements of the plan include: a) agreement to taper, b) education on expected symptoms during the taper, c) return visits for intolerable symptoms with consideration of a pause in the taper, and d) other treatments to be changed or substituted.
2. The provider should be supportive and engaged in the patient's care, management, and concerns. Do not "abandon" the patient. Consider engaging the patient in other active therapies during taper, such as CBT, progressive active aerobic and strengthening exercises, education, psychiatric consultation, or psychiatric medication (e.g., buspirone, antidepressant, hydroxyzine, pregabalin, propranolol, quetiapine).
3. Rate of tapering is typically 5-10% per week. Brief negotiated pauses in the rate of a taper are acceptable.
4. Educate the patient that tapering may produce symptoms such as anxiety, insomnia, emotional distress, headaches, nausea, and sweating. These symptoms are expected and not contraindications to a taper (although if intolerable, they may be a rationale for a brief pause in a taper).

5. The taper should be stopped if there is objective worsening of function, excessive withdrawal, and/or intolerance. After stabilization, resumption of the taper should be attempted. However, if there is a plateau level where function is achieved, that dose should be noted in the records and maintained for an ongoing basis. There is consideration for reattempting tapering in subsequent years.

Harms:

Withdrawal symptoms, including headache, nausea, palpitations, hyperventilation, sweating, anxiety, panic attacks, insomnia, irritability, mood changes, hallucinations, seizures depression, visual disturbances, muscle spasms, tremors, and rare fatalities [1370]

Benefits:

Reduce risk of adverse events, improved CNS higher cortical functions, reduced risk of motor vehicle crashes and medication-related deaths

Rationale:

The overall quality of the literature to address comparative effectiveness is fairly limited [1371]. One moderate-quality trial found CBT in addition to tapering superior to tapering alone and also documented the improved outcomes persisted at 12 months in 24% vs. 70% [1358]. A RCT found a higher success rate for tapering associated with use of imipramine (82.6%) followed by buspirone (67.9%) and placebo (37.5%) [1359]. A 3-year cluster randomized study found a specific tapering regimen superior to no specific training of the providers [1372, 1373], although the 3-year success rate was modestly better at 39-41% vs. 26% [1373]. Another trial found buspirone superior to placebo for tapering and resulted in milder rebound anxiety and withdrawal symptoms [1142]. Tapering and discontinuation of benzodiazepines has generally low adverse effects if accomplished with experienced tapering and careful monitoring (although some patients have difficulty with tapering), is low cost, and is recommended.

Evidence:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Withdrawal, Tapering, Benzodiazepines; anxiety, anxiety disorders, panic disorder, phobic disorder, phobic disorders, phobia; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, prospective studies; not pediatric, and not adolescents. We found and reviewed 2170 articles in PubMed, 3811 in Scopus, 28 in CINAHL, 139 in Cochrane Library, 18000 in Google Scholar, and 7 from other sources[†]. We considered for inclusion 9 from PubMed, 0 from Scopus, 1 from CINAHL, 1 from Cochrane Library, 4 from Google Scholar, and 7 from other sources. Of the 23 articles considered for inclusion, 14 randomized trials and 1 systematic review met the inclusion criteria.

[†] The results for databases are sorted by relevancy based on customized search term algorithms. Algorithms for each database determine relevancy. The first 100 articles are reviewed in each search, and if relevant literature appears in the first 100 articles, we review an additional 100 articles. If relevant articles appear in these additional 100 articles, we then review another 100. We continue this pattern of review until we review a batch of 100 articles that contains no relevant literature. When this happens then the remaining articles are not reviewed due to a lack of relevancy.

Pregabalin for Benzodiazepine Tapering and Discontinuation

Recommended.

Pregabalin is recommended for benzodiazepine tapering and discontinuation.

Strength of Evidence – Recommended, Evidence (C)

Level of Confidence – Low

<i>Indications:</i>	Patients being tapered from benzodiazepines
<i>Benefits:</i>	Reduced anxiety compared with placebo and likely increased long-term successful BZD-free status
<i>Harms:</i>	Risk of remission, otherwise usual risks associated with pregabalin
<i>Frequency/Dose/Duration:</i>	Pregabalin 150 mg/day titrated up to 600 mg/day [1369]
<i>Indications for Discontinuation:</i>	Rate of taper may need to be slowed based on degree of symptoms. Intolerance or adverse effects may result in need to stop the use of pregabalin and/or implementation of another medication.
<i>Rationale:</i>	One moderate-quality trial suggested pregabalin is effective for BZD tapering and discontinuation [1369]; thus, pregabalin is recommended for use in tapering.

Odansetron for Benzodiazepine Tapering and Discontinuation

Not Recommended.

Odansetron is not recommended for benzodiazepine tapering and discontinuation.

Strength of Evidence – Not Recommended, Evidence (C)

Level of Confidence – Low

<i>Rationale:</i>	One moderate-quality trial suggested odansetron is ineffective for BZD tapering and discontinuation [1374]; thus, odansetron is not recommended for tapering.
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Electroacupuncture for Benzodiazepine Tapering and Discontinuation

Not Recommended.

Electroacupuncture is not recommended for benzodiazepine tapering and discontinuation.

Strength of Evidence – Not Recommended, Evidence (C)

Level of Confidence – Low

<i>Rationale:</i>	One moderate-quality trial suggested electroacupuncture is ineffective for BZD tapering and discontinuation [1366]; thus, acupuncture is not recommended for tapering.
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Appendix 1: PICO Questions

Screening and Testing:

- P** Workers and/or patients with suspected anxiety
 - I** Anxiety disorders screening tools
 - C** What is the quality evidence supporting the use of anxiety disorders screening tools?
 - O** Identification of anxiety and/or associated symptoms
-
- P** Workers and/or patients with suspected anxiety
 - I** Psychometric testing
 - C** What is the quality evidence supporting the use of psychometric testing?
 - O** Identification of anxiety and/or associated symptoms
-
- P** Workers and/or patients with suspected anxiety
 - I** Pharmacogenomic testing
 - C** Is there quality evidence supporting the use of pharmacogenomic testing?
 - O** Identification of anxiety and/or associated symptoms

EDUCATION:

- P** Workers and/or patients with anxiety
- I** Education
- C** What is the quality evidence supporting the use of education?
- O** Improved anxiety and/or associated symptoms

EXERCISE:

- P** Workers and/or patients with anxiety
 - I** Aerobic exercise
 - C** Is aerobic exercise superior to sham or equivalent to other treatments?
 - O** Improved anxiety and/or associated symptoms
-
- P** Workers and/or patients with anxiety
 - I** Strengthening exercises
 - C** Are strengthening exercise superior to sham or equivalent to other treatments?
 - O** Improved anxiety and/or associated symptoms
-
- P** Workers and/or patients with anxiety
 - I** Flexibility exercises
 - C** Are flexibility exercises superior to sham or equivalent to other treatments?
 - O** Improved anxiety and/or associated symptoms
-
- P** Workers and/or patients with anxiety
 - I** Yoga
 - C** Is yoga superior to sham, or equivalent to other effective treatments?
 - O** Improved anxiety and/or associated symptoms

BEHAVIORAL AND PSYCHOLOGICAL INTERVENTIONS:

- P** Workers and/or patients with anxiety
I Cognitive behavioral therapy (CBT)
C Is CBT superior to sham, or equivalent to other effective treatments?
O Improved anxiety and/or associated symptoms
- P** Workers and/or patients with anxiety
I Computer-assisted cognitive behavioral therapy
C Is computer-assisted cognitive behavioral therapy superior to sham, or equivalent to other effective treatments?
O Improved anxiety and/or associated symptoms
- P** Workers and/or patients with anxiety
I Dialectical behavioral therapy (DBT)
C Is DBT superior to sham, or equivalent to other effective treatments?
O Improved anxiety and/or associated symptoms
- P** Workers and/or patients with anxiety
I Acceptance and commitment therapy or interpersonal therapy
C Is acceptance and commitment therapy or interpersonal therapy superior to sham, or equivalent to other effective treatments?
O Improved anxiety and/or associated symptoms
- P** Workers and/or patients with anxiety
I Bibliotherapy/cognitive bibliotherapy
C Is bibliotherapy/cognitive bibliotherapy superior to sham, or equivalent to other effective treatments?
O Improved anxiety and/or associated symptoms
- P** Workers and/or patients with anxiety
I CBT with antidepressants
C Is CBT with antidepressants superior to sham, or equivalent to other effective treatments?
O Improved anxiety and/or associated symptoms
- P** Workers and/or patients with anxiety
I Insight-oriented therapies inclusive of short-term psychosocial psychotherapy
C Are insight-oriented therapies (including short-term psychosocial psychotherapy) superior to sham, or equivalent to other effective treatments?
O Improved anxiety and/or associated symptoms
- P** Workers and/or patients with anxiety
I Stress inoculation training
C Is stress inoculation training superior to sham, or equivalent to other effective treatments?
O Improved anxiety and/or associated symptoms

- P** Workers and/or patients with anxiety
I Stress management (behavioral/cognitive/physical)
C Is stress management superior to sham, or equivalent to other effective treatments?
O Improved anxiety and/or associated symptoms
- P** Workers and/or patients with anxiety
I Supportive therapy
C Is supportive therapy superior to sham, or equivalent to other effective treatments?
O Improved anxiety and/or associated symptoms
- P** Workers and/or patients with anxiety
I Distractive therapy
C Is distractive therapy an effective treatment for anxiety?
O Improved anxiety and/or associated symptoms
- P** Workers and/or patients with anxiety
I Exposure therapy and prolonged exposure therapy for stress relief
C Are either exposure therapy or prolonged exposure therapy superior to sham, or equivalent to other effective treatments?
O Improved anxiety and/or associated symptoms
- P** Workers and/or patients with anxiety
I Virtual reality exposure therapy
C Is virtual reality exposure therapy an effective treatment for anxiety?
O Improved anxiety and/or associated symptoms
- P** Workers and/or patients with anxiety
I Meditation, mindfulness, and relaxation techniques
C Are meditation, mindfulness, or relaxation techniques effective in the treatment of anxiety?
O Improved anxiety and/or associated symptoms
- P** Workers and/or patients with anxiety
I Emotional freedom therapy
C Is emotional freedom therapy superior to sham, or equivalent to other effective treatments for anxiety?
O Improved anxiety and/or associated symptoms
- MEDICATIONS:**
- P** Workers and/or patients with anxiety
I Antidepressants
C Are antidepressants superior to sham, or equivalent to other effective treatments?
O Improved anxiety and/or associated symptoms
- P** Workers and/or patients with anxiety
I Anxiolytics and benzodiazepines
C Are anxiolytics and/or benzodiazepines superior to sham, or equivalent to other effective treatments?
O Improved anxiety and/or associated symptoms

- P** Workers and/or patients with anxiety
- I** Buspirone
- C** Is buspirone superior to sham, or equivalent to other effective treatments?
- O** Improved anxiety and/or associated symptoms

- P** Workers and/or patients with anxiety
- I** Antipsychotics (quetiapine)
- C** Are antipsychotics including quetiapine superior to sham, or equivalent to other effective treatments?
- O** Improved anxiety and/or associated symptoms

- P** Workers and/or patients with anxiety
- I** Propranolol
- C** Is propranolol superior to sham, or equivalent to other effective treatments?
- O** Improved anxiety and/or associated symptoms

- P** Workers and/or patients with anxiety
- I** Atenolol
- C** Is atenolol superior to sham, or equivalent to other effective treatments?
- O** Improved anxiety and/or associated symptoms

- P** Workers and/or patients with anxiety
- I** Gabapentin
- C** Is gabapentin superior to sham, or equivalent to other effective treatments?
- O** Improved anxiety and/or associated symptoms

- P** Workers and/or patients with anxiety
- I** Pregabalin
- C** Is pregabalin superior to sham, or equivalent to other effective treatments?
- O** Improved anxiety and/or associated symptoms

- P** Workers and/or patients with anxiety
- I** Valproic acid
- C** Is valproic acid superior to sham, or equivalent to other effective treatments?
- O** Improved anxiety and/or associated symptoms

- P** Workers and/or patients with anxiety
- I** Hydroxyzine
- C** Is hydroxyzine superior to sham, or equivalent to other effective treatments?
- O** Improved anxiety and/or associated symptoms

MISCELLANEOUS MEDICAL THERAPIES, INCLUDING NUTRACEUTICALS, VITAMINS, AND ALLIED THERAPIES:

- P** Workers and/or patients with anxiety
- I** Nutraceuticals
- C** Is there quality evidence supporting the use of nutraceuticals in the treatment of anxiety?
- O** Improved anxiety and/or associated symptoms

- P** Workers and/or patients with anxiety
 - I** St. John's wort (*Hypericum perforatum*)
 - C** Is St. John's wort (*Hypericum perforatum*) superior to sham, or equivalent to other effective treatments for anxiety?
 - O** Improved anxiety and/or associated symptoms
- P** Workers and/or patients with anxiety
 - I** Kava extract
 - C** Is there quality evidence for using kava extract as an effective treatment for anxiety?
 - O** Improved anxiety and/or associated symptoms
- P** Workers and/or patients with anxiety
 - I** Lavender oil (*Silexan*)
 - C** Is there quality evidence for the use of lavender oil (*Silexan*) in the treatment of anxiety?
 - O** Improved anxiety and/or associated symptoms
- P** Workers and/or patients with anxiety
 - I** Valerian
 - C** Is valerian an effective treatment for anxiety?
 - O** Improved anxiety and/or associated symptoms
- P** Workers and/or patients with anxiety
 - I** Marijuana, cannabis, cannabinoids, and cannabidiol
 - C** Are marijuana, cannabis, cannabinoids, and/or cannabidiol effective in the treatment of anxiety?
 - O** Improved anxiety and/or associated symptoms

NON-INVASIVE MAGNETIC THERAPIES, ACUPUNCTURE, ACUPRESSURE, THERAPEUTIC TOUCH, AND MASSAGE:

- P** Workers and/or patients with anxiety
 - I** Transcranial magnetic stimulation and repetitive transcranial magnetic stimulation (RTMS)
 - C** Is transcranial magnetic stimulation and repetitive transcranial magnetic stimulation (RTMS) superior to sham, or equivalent to other effective treatments?
 - O** Improved anxiety and/or associated symptoms
- P** Workers and/or patients with anxiety
 - I** Brainwave synchronization
 - C** Is brainwave synchronization superior to sham, or equivalent to other effective treatments?
 - O** Improved anxiety and/or associated symptoms
- P** Workers and/or patients with anxiety
 - I** Acupressure
 - C** Is acupressure superior to sham, or equivalent to other effective treatments?
 - O** Improved anxiety and/or associated symptoms
- P** Workers and/or patients with anxiety
 - I** Acupuncture

- C** Is acupuncture superior to sham, or equivalent to other effective treatments?
- O** Improved anxiety and/or associated symptoms

- P** Workers and/or patients with anxiety
- I** Therapeutic touch
- C** Is therapeutic touch superior to sham, or equivalent to other effective treatments?
- O** Improved anxiety and/or associated symptoms

- P** Workers and/or patients with anxiety
- I** Massage
- C** Is massage superior to sham, or equivalent to other effective treatments?
- O** Improved anxiety and/or associated symptoms

PHYSICAL MEDICINE:

- P** Workers and/or patients with anxiety
- I** Physical medicine
- C** Is physical medicine superior to placebo, or equivalent to other effective treatments for treatment of anxiety?
- O** Improved anxiety and/or associated symptoms

BENZODIAZEPINE TAPERING AND DISCONTINUATION:

- P** Workers and/or patients with anxiety dependent on benzodiazepines
- I** Benzodiazepine discontinuation and tapering
- C** Is there quality evidence to support benzodiazepine discontinuation and tapering in effective treatment of anxiety related benzodiazepine dependence?
- O** Improved anxiety and/or associated symptoms without significant withdrawal symptoms

- P** Workers and/or patients with anxiety dependent upon benzodiazepines
- I** Pregabalin
- C** Is there quality evidence to support the use of pregabalin for successful benzodiazepine tapering and/or discontinuation?
- O** Improved anxiety and/or associated symptoms without significant withdrawal symptoms

- P** Workers and/or patients with anxiety dependent on benzodiazepines
- I** Ondansetron
- C** Is there quality evidence to support the use of ondansetron for successful benzodiazepine tapering and/or discontinuation?
- O** Improved anxiety and/or associated symptoms without significant withdrawal symptoms

- P** Workers and or patients with anxiety dependent upon benzodiazepines
- I** Electroacupuncture
- C** Is there quality evidence to support electroacupuncture for successful benzodiazepine tapering and/or discontinuation?
- O** Improved anxiety and/or associated symptoms without significant withdrawal symptoms

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