AMERICAN COLLEGE OF OCCUPATIONAL AND ENVIRONMENTAL MEDICINE

Anxiety Disorders

Effective Date: April 30, 2021

CONTRIBUTORS

Editor-in-Chief:
Kurt T. Hegmann, MD, MPH, FACOEM, FACP

Evidence-based Practice Workplace Mental Health Panel Co-Chairs:
Daniel Bruns, PsyD, FAPA
Pamela A. Warren, PhD

Evidence-based Practice Workplace Mental Health Panel Members:
Tony Alleman, MD, MS, MPH
Molly M. Brady, PsyD
Garson M. Caruso, MD, MPH, FACOEM, FIAIME
Gregory P. Couser, MD, MPH
Brad K. Grunert, PhD
Harold E. Hoffman, MD, CCFP, FCRP, FRCPC
Mark H. Hyman, MD, FACP, FIAIME
Les Kertay, PhD, ABPP
Steven Mandel, MD, FACOEM, FAAN, FAADEP
Yusef Sayeed, MD, MPH, Meng, CPH, CMRO, CME, COHC, EIT, DABPM
Joel S. Steinberg, MD

Panel members for the multidisciplinary Workplace Mental Health Guideline represent expertise in addiction medicine, clinical psychology, educational psychology, forensic psychiatry, internal medicine, neurology, occupational medicine, preventive medicine, psychiatry, and psychology. As required for quality guidelines (Institute of Medicine's (IOM) Standards for Developing Trustworthy Clinical Practice Guidelines and Appraisal of Guidelines for Research and Evaluation (AGREE)), a detailed application process captured conflicts of interest. The above panel has none to declare relevant to this guideline.

Panel Consultant:
Donald C. Sinclair II, JD

Methodology Committee Consultant:
Nelson S. Haas, MD, MPH, MA, FACOEM

Copyright ©2021 Reed Group, Ltd.
Available on http://www.mdguidelines.com

Research Conducted By:
Kurt T. Hegmann, MD, MPH, FACOEM, FACP
Kristine Hegmann, MSPH, CIC
Matthew S. Thiese, PhD, MSPH
Emilee Eden, BS, MPH
Jenna L. Praggastis, BS
Harkomal Kaur, BS
Michael L. Northrup, BS
Skyler D. Walker, BS
Chapman B. Cox
Jenny Dang
Melissa Gonzalez
Weijun Yu, BM, BA, MS
Vivian Nguyen
Matthew Houston, BS
Helena Tremblay

Specialty Society and Society Representative Listing

ACOEM acknowledges the following organizations and their representatives who served as reviewers of the Anxiety Disorders Guideline. Their contributions are greatly appreciated. By listing the following individuals or organizations, it does not infer that these individuals or organizations support or endorse the Anxiety Disorders Guideline developed by ACOEM.

American College of Physicians
Stephen Mohring, MD, FACP

American College of Preventive Medicine
James A. Tacci, MD, JD, MPH, FACPM, FACOEM

American Occupational Therapy Association
Elizabeth Griffin Lannigan, PhD, OTR/L, FAOTA

American Physical Therapy Association

American Psychological Association
Lynn F. Bufka, PhD

Copyright ©2021 Reed Group, Ltd.

Table of Contents

Copyright ©2021 Reed Group, Ltd.

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)

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

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:

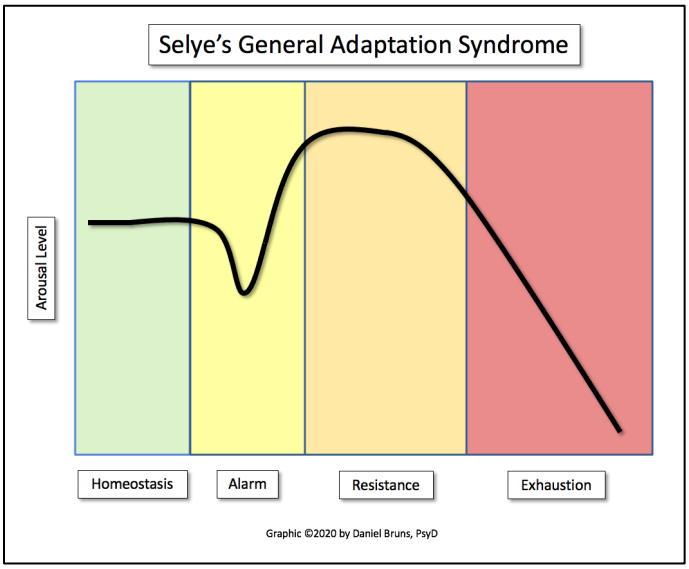
1. The first stage of GAS consists of a shock reaction that disrupts the organism's homeostasis. Initially, stage 1A involves decreased resistance by the organism, which

Copyright ©2021 Reed Group, Ltd.

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."



Copyright ©2021 Reed Group, Ltd.

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].

Copyright ©2021 Reed Group, Ltd.

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 disregulation 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

Copyright ©2021 Reed Group, Ltd.

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 kinesiophobia [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].

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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)

Copyright ©2021 Reed Group, Ltd.

[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].

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

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.,

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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,

Copyright ©2021 Reed Group, Ltd.

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].

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

		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.	

* 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.

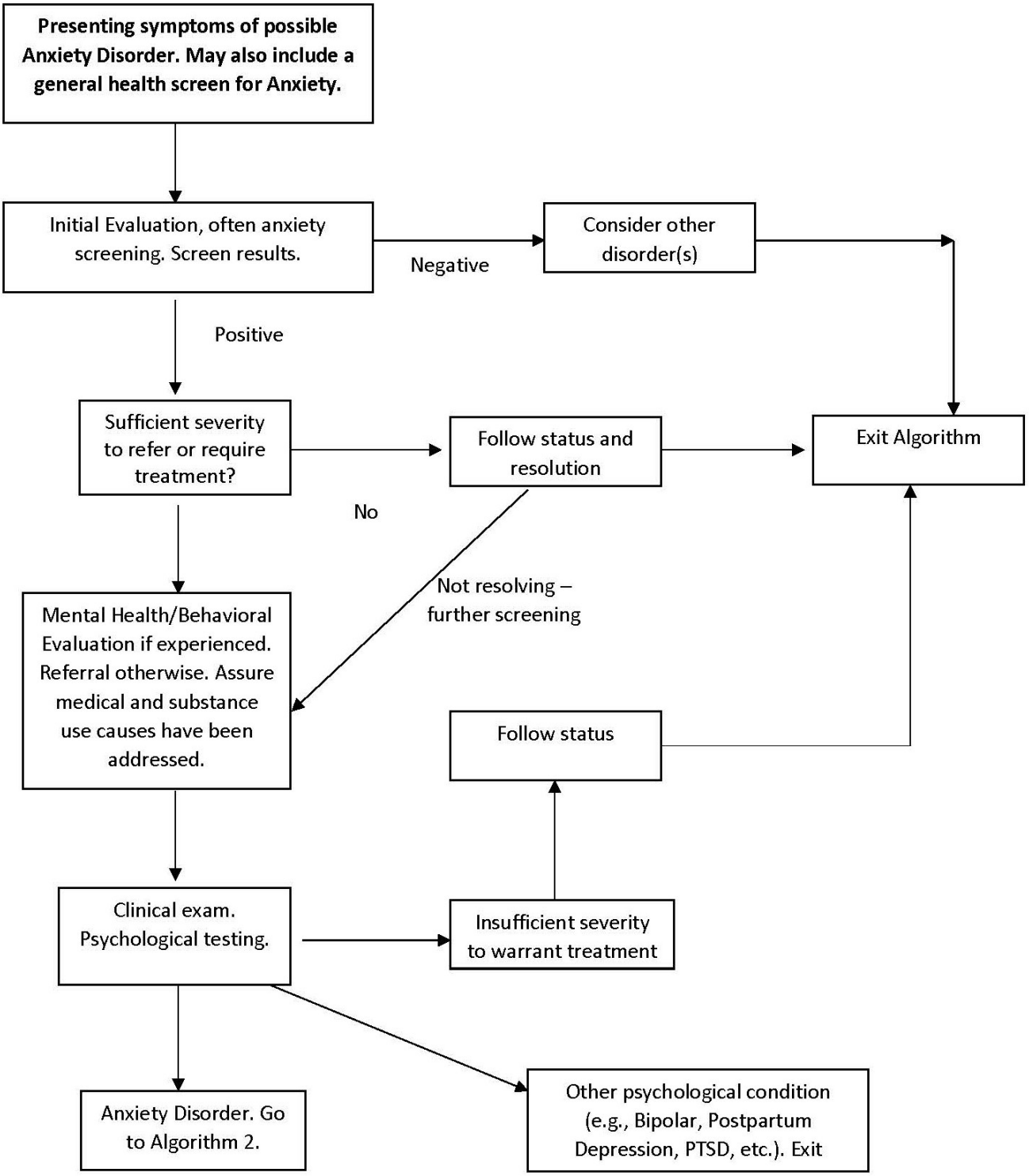
†A person should already have received effective, evidence-based treatment and be stable. Thus, it should be quite rare that someone would continue to have severe symptoms at 3 months. RTW/SAW is nearly always successful. Greater intensity of treatment, interaction with the employer, and plans to address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

Copyright ©2021 Reed Group, Ltd.

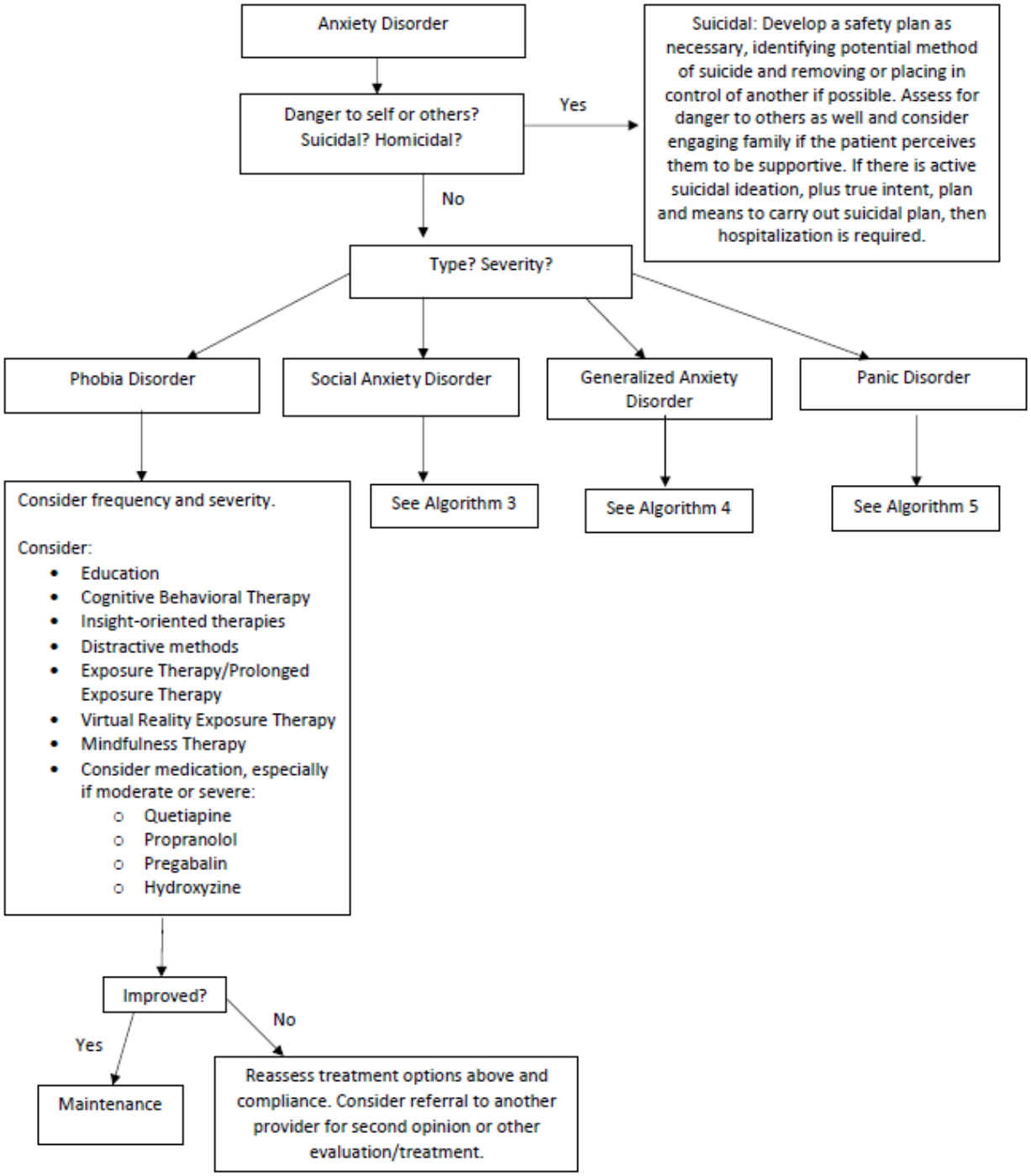
Algorithms

Algorithm 1. Presenting Symptoms of Possible Anxiety Disorder



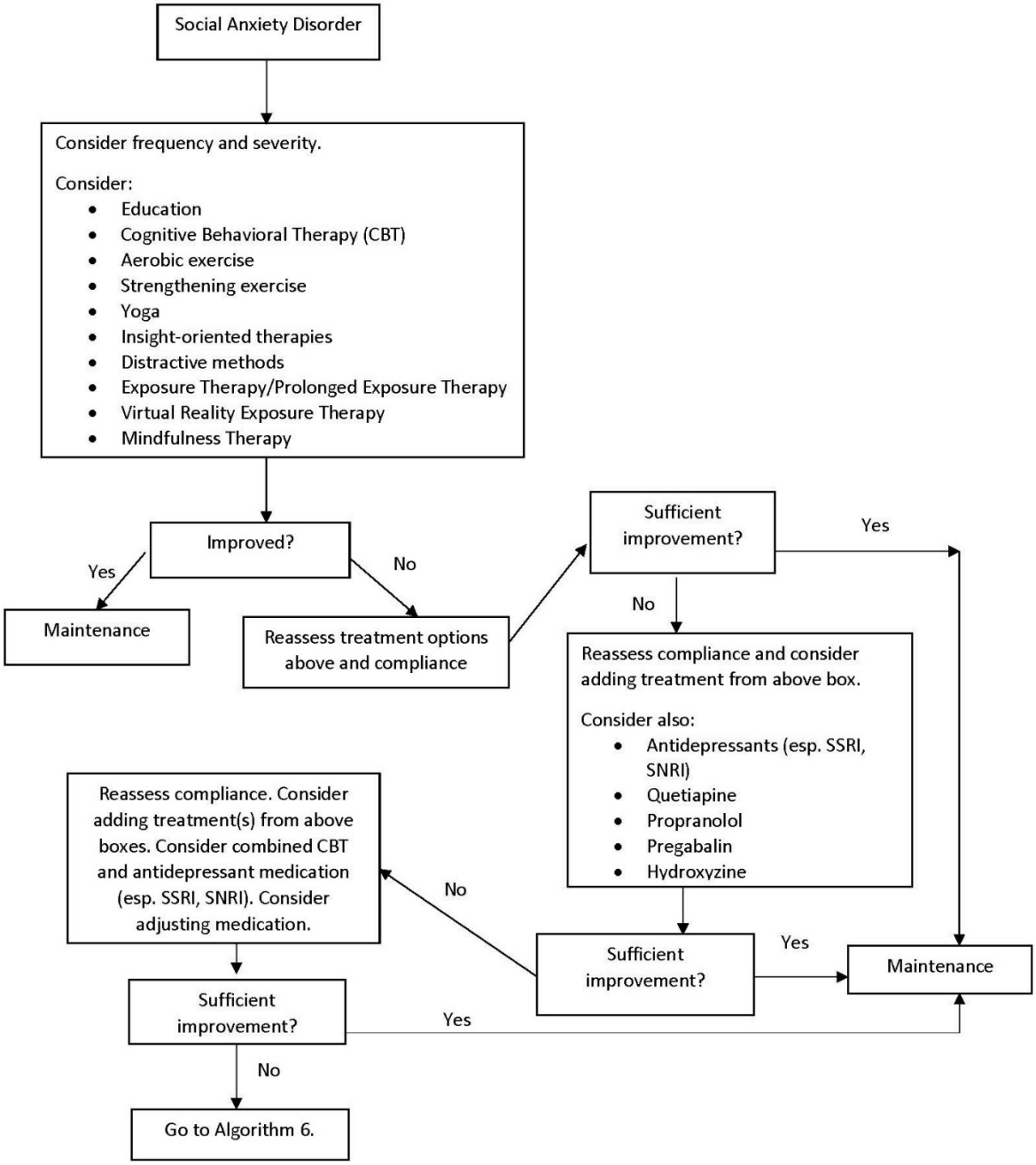
Copyright ©2021 Reed Group, Ltd.

Algorithm 2. Management of Anxiety Disorder by Type



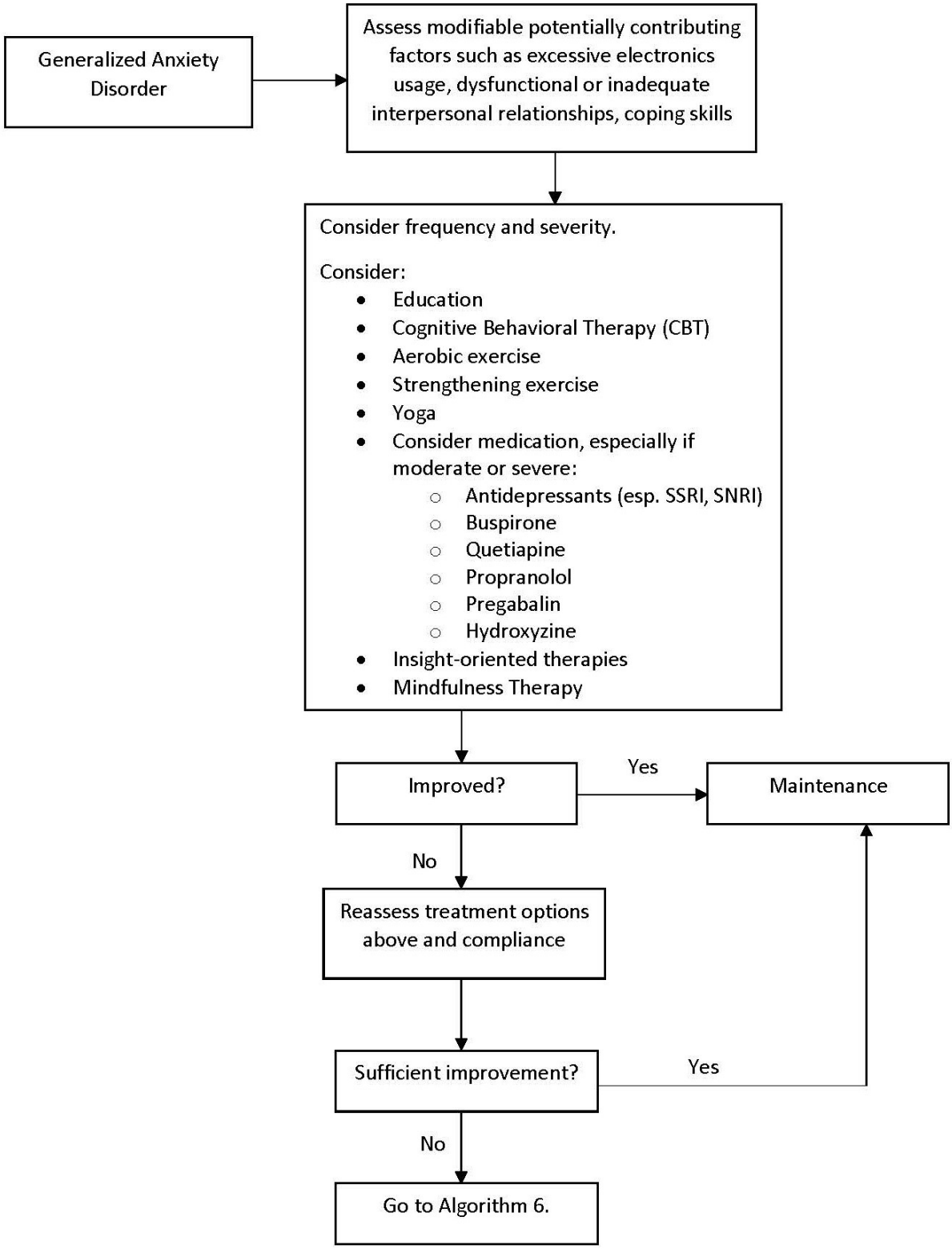
Copyright ©2021 Reed Group, Ltd.

Algorithm 3. Management of Social Anxiety Disorder



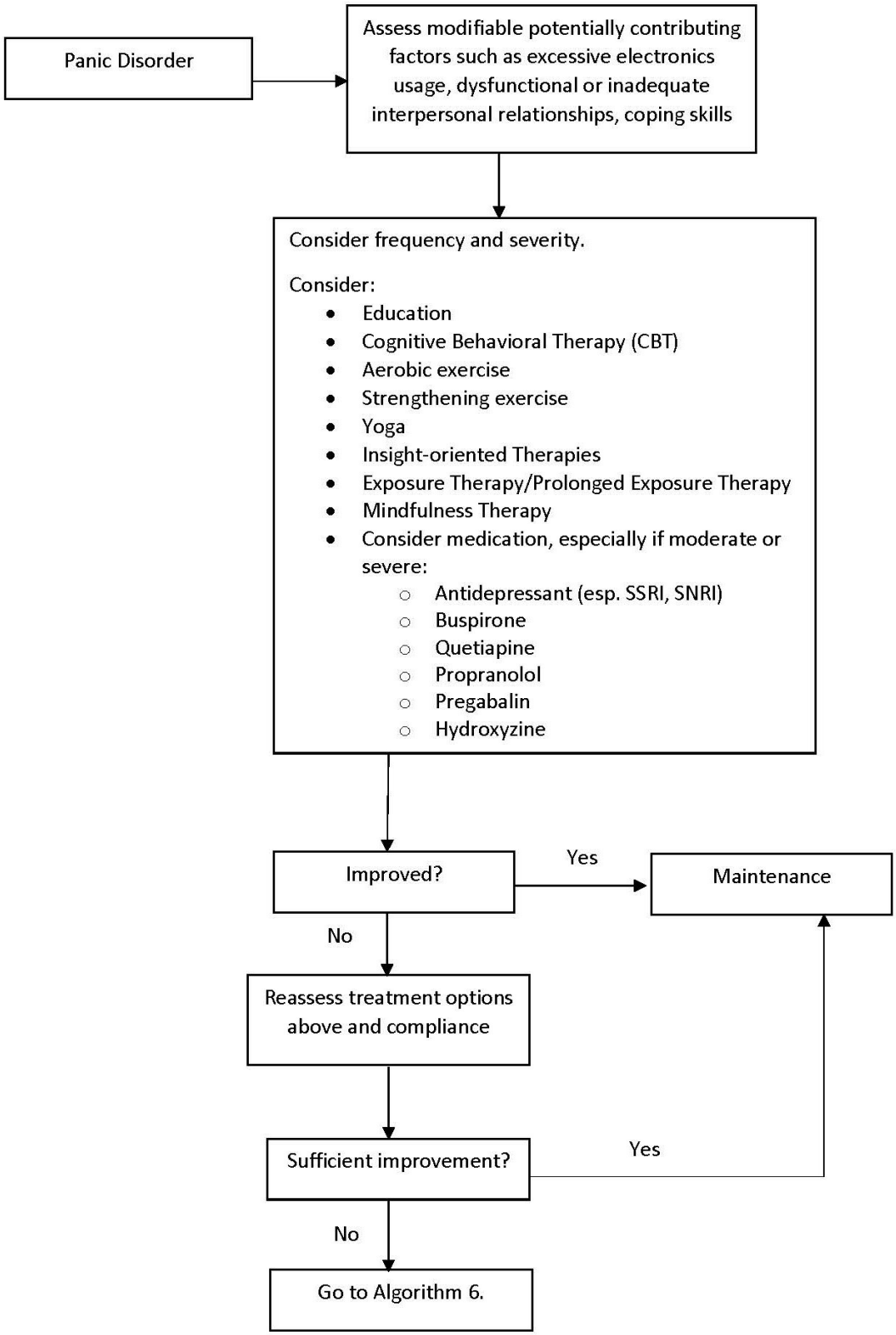
Copyright ©2021 Reed Group, Ltd.

Algorithm 4. Management of Generalized Anxiety Disorder



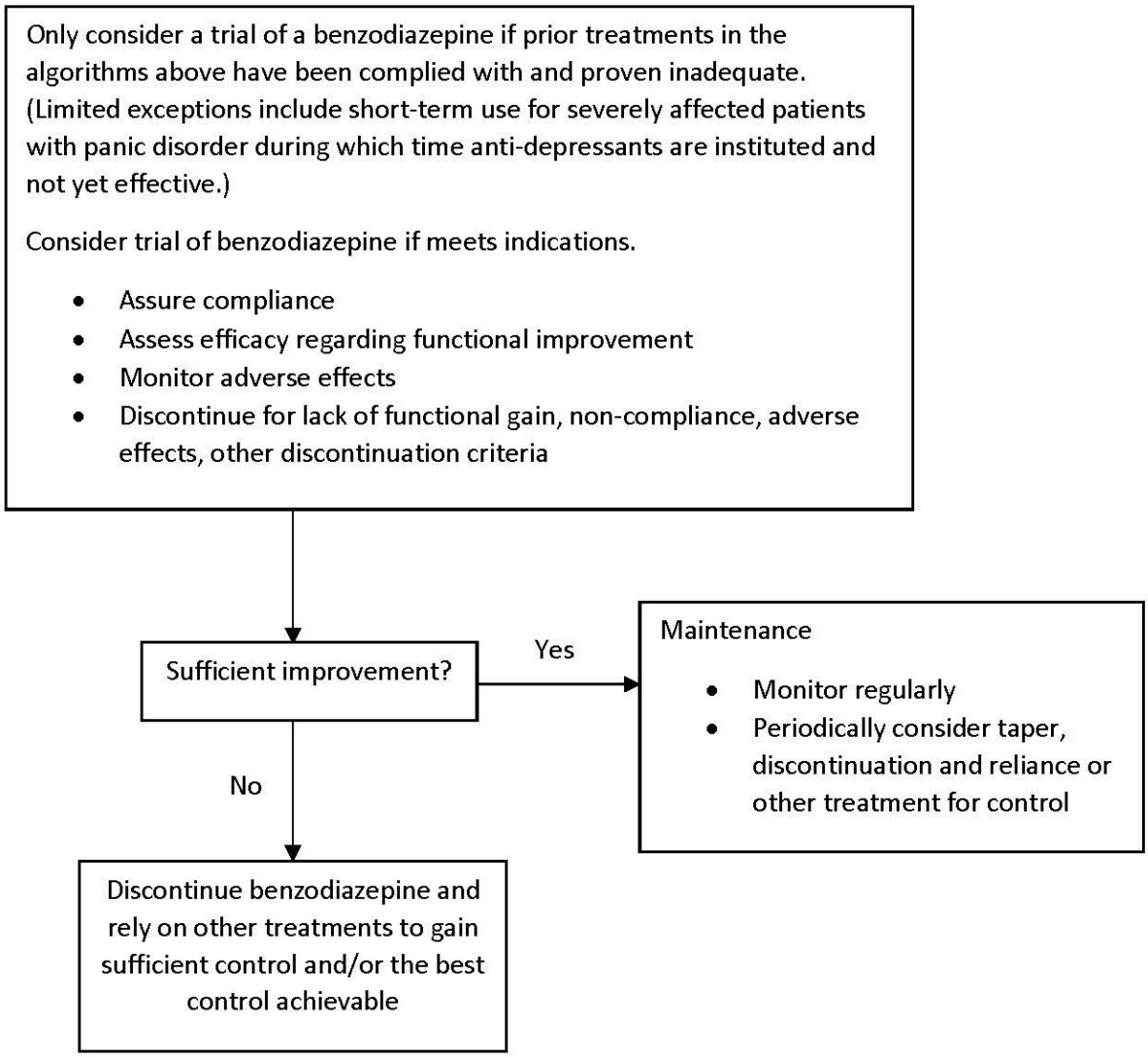
Copyright ©2021 Reed Group, Ltd.

Algorithm 5. Management of Panic Disorder



Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

- 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

Copyright ©2021 Reed Group, Ltd.

- 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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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 bums 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).

Copyright ©2021 Reed Group, Ltd.

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."

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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 phobics, 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

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

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**

Indications:	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.
Benefits:	Earlier identification of potential anxiety disorders; assists with directing the patient to appropriate mental health services that include diagnostic confirmation.
Harms:	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.
Frequency/Dose/Duration:	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.
Rationale:	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.
Evidence:	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.

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

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 different 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

Copyright ©2021 Reed Group, Ltd.

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**

Indications:	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.
Benefits:	Provide psychometric evidence regarding potential for anxiety disorders and especially for other mental health disorder(s).
Harms:	Negligible
Frequency/Dose/Duration:	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].
Rationale:	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].
Evidence:	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

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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

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

Evidence: 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

Frequency/Dose/Duration:	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.
Indications for Discontinuation:	Sufficient understanding of anxiety, resolution of symptoms, non-compliance.
Rationale:	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.
Evidence:	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.

Copyright ©2021 Reed Group, Ltd.

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.
Benefits:	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].
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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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**

Indications:	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.
Benefits:	Improvements in symptoms of anxiety. Increased flexibility, posture, and overall well-being.
Harms:	Negligible, muscle soreness
Frequency/Dose/Duration:	Twice-weekly, 1-hour sessions of yoga for 2 months; results were better if combined with a comparable schedule of CBT [580].
Indications for Discontinuation:	Lack of anxiety symptom improvement or sufficient improvement to not warrant further sessions, noncompliance, intolerance.
Rationale:	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.
Evidence:	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.

Copyright ©2021 Reed Group, Ltd.

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**

Copyright ©2021 Reed Group, Ltd.

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. 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].
Benefits:	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].

Copyright ©2021 Reed Group, Ltd.

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 heterogenous populations, rather than pure anxiety patients, resulting in no quality evidence of efficacy and thus no recommendation.

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.

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 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

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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**

Indications:	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.
Benefits:	Improvement in anxiety symptoms
Harms:	Increased symptoms, intolerance
Frequency/Dose/Duration:	One trial used 24 sessions of 50-minute duration, twice weekly for 12 weeks [643].
Indications for Discontinuation:	Resolution of symptoms, non-compliance, lack of efficacy, or adverse events
Rationale:	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.
Evidence:	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: There are no quality trials and thus 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: 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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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**

Indications:	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.
Benefits:	Improvement in anxiety symptoms
Harms:	Increased symptoms, intolerance
Frequency/Dose/Duration:	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].
Indications for Discontinuation:	Resolution of symptoms, non-compliance, lack of efficacy, or adverse events
Rationale:	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.
Evidence:	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

Copyright ©2021 Reed Group, Ltd.

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**

Indications:	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.
Benefits:	Improvement in anxiety symptoms
Harms:	Increased symptoms, intolerance
Frequency/Dose/Duration:	The highest-quality trial administered 12 weekly treatment sessions with 3 booster sessions after treatment [683].
Indications for Discontinuation:	Resolution of symptoms, non-compliance, lack of efficacy, or adverse events
Rationale:	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.
Evidence:	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**

Indications:	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.
Benefits:	Improvement in anxiety symptoms
Harms:	Increased symptoms, intolerance
Frequency/Dose/Duration:	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.
Indications for Discontinuation:	Resolution of symptoms, non-compliance, lack of efficacy, or adverse events
Rationale:	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

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).

Evidence: 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).

Copyright ©2021 Reed Group, Ltd.

Benefits:	Improvement in anxiety symptoms
Harms:	Negligible
Frequency/Dose/Duration:	Weekly 2.5-hour sessions for 8 weeks of mindfulness therapy [574]
Indications for Discontinuation:	Symptom resolution or lack of efficacy
Rationale:	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.
Evidence:	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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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**

Indications:	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].
Benefits:	Improvements in anxiety symptoms, improved function, and reduced relapses.
Harms:	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

Copyright ©2021 Reed Group, Ltd.

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].

Copyright ©2021 Reed Group, Ltd.

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 heartrate, 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].

Despiramine: 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].

Copyright ©2021 Reed Group, Ltd.

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 heartrate, 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,

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

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, Narldelzine: 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,

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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 anti-depressants 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

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

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, 5431in 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*,

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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**

Indications:	Anxiety disorders, especially GAD (for which there is the most consistent evidence of efficacy)
Benefits:	Reduced anxiety symptoms
Harms:	Drowsiness, dizziness, chest pain, confusion, palpitations, incoordination, weakness, fatigue, nervousness, restlessness.
Frequency/Dose/Duration:	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.
Indications for Discontinuation:	Intolerability, adverse effects, non-compliance, lack of efficacy.
Rationale:	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.
Evidence:	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.

Copyright ©2021 Reed Group, Ltd.

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**

Indications:	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.
Benefits:	Improvements in anxiety symptoms, sleep, and function
Harms:	Dizziness, faintness, lightheadedness, drowsiness, chills, sleepiness, drowsiness, fatigue, diarrhea, constipation, blurred vision, dry mouth.
Frequency/Dose/Duration:	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].
Indications for Discontinuation:	Intolerability, adverse effects, non-compliance, lack of efficacy
Rationale:	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.
Evidence:	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

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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**

Indications:	Generalized anxiety and other anxiety disorders. Generally should have had treatment with CBT, aerobic exercise, and strengthening exercises. May be used in combination.
Benefits:	Improved anxiety symptoms. Antihypertensive properties may be used for an advantage, although those properties also produce some of the adverse effects.
Harms:	Drowsiness, slow heart rate, syncope, heart block, diarrhea, dry eyes, weakness, tiredness, rash, sleeping disturbance, muscle cramps, swollen ankles
Frequency/Dose/Duration:	Propranolol 40 mg QID [1166]
Indications for Discontinuation:	Resolution of anxiety symptoms, adverse effects, non-compliance
Rationale:	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.
Evidence:	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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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

Pregabalin

Moderately Recommended.

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

Strength of Evidence – **Moderately Recommended, Evidence (B)**
Level of Confidence – **Moderate**

Indications:	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.
Benefits:	Improved anxiety symptoms with relatively early onset of action. Few rebound anxiety problems after discontinuation [1182].
Harms:	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.
Frequency/Dose/Duration:	Pregabalin 400 mg/day is effective and has less adverse effects compared with pregabalin 600 mg/day [1015]
Indications for Discontinuation:	Resolution of anxiety symptoms, adverse effects, non-compliance
Rationale:	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.
Evidence:	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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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**

Indications:	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.
Benefits:	Reduces anxiety symptoms and causes sedative effects, which may be selectively beneficial
Harms:	Sedative effects. Paradoxical increased anxiety. Generally not indicated for patients with safety-critical work.
Frequency/Dose/Duration:	Hydroxyzine 12.5 mg every morning, 12.5 mg at noon, and 50 mg at bedtime.
Indications for Discontinuation:	Resolution of anxiety symptoms, intolerance, non-compliance, excessive adverse effects.
Rationale:	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).
Evidence:	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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

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).

Copyright ©2021 Reed Group, Ltd.

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.

Copyright ©2021 Reed Group, Ltd.

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**

Indications:	Patients being tapered from benzodiazepines
Benefits:	Reduced anxiety compared with placebo and likely increased long-term successful BZD-free status
Harms:	Risk of remission, otherwise usual risks associated with pregabalin
Frequency/Dose/Duration:	Pregabalin 150 mg/day titrated up to 600 mg/day [1369]
Indications for Discontinuation:	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.
Rationale:	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**

Rationale:	One moderate-quality trial suggested odansetron is ineffective for BZD tapering and discontinuation [1374]; thus, odansetron is not recommended for tapering.

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**

Rationale:	One moderate-quality trial suggested electroacupuncture is ineffective for BZD tapering and discontinuation [1366]; thus, acupuncture is not recommended for tapering.

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

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

Copyright ©2021 Reed Group, Ltd.

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 Odansetron
C Is there quality evidence to support the use of odansetron 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

Copyright ©2021 Reed Group, Ltd.

References

1. Craske, M.G., et al., *Anxiety disorders.* Nature Reviews Disease Primers, 2017. **3**(1): p. 17024.

2. Goldstein-Piekarski, A., L. Williams, and K. Humphreys, *A trans-diagnostic review of anxiety disorder comorbidity and the impact of multiple exclusion criteria on studying clinical outcomes in anxiety disorders.* Translational psychiatry, 2016. **6**(6): p. e847-e847.

3. ADAA. *Highlights: Workplace Stress & Anxiety Disorders Survey*. 2018; Available from: https://adaa.org/workplace-stress-anxiety-disorders-survey.

4. Kessler, R.C., et al., *Lifetime prevalence and age-of-onset distributions of mental disorders in the World Health Organization's World Mental Health Survey Initiative.* World psychiatry : official journal of the World Psychiatric Association (WPA), 2007. **6**(3): p. 168-176.

5. NIMH. *Any Anxiety Disorder*. 2017; Available from: https://www.nimh.nih.gov/health/statistics/any-anxiety-disorder.shtml#:~:text=Prevalence%20of%20Any%20Anxiety%20Disorder%20Among%20Adults,-Based%20on%20diagnostic&text=An%20estimated%2019.1%25%20of%20U.S.,than%20for%20males%20(14.3%25).

6. Bandelow, B., et al., *Efficacy of treatments for anxiety disorders: a meta-analysis.* International Clinical Psychopharmacology, 2015. **30**(4): p. 183-192.

7. Lewis-Fernández, R., et al., *Culture and the anxiety disorders: recommendations for DSM-V.* Depress Anxiety, 2010. **27**(2): p. 212-29.

8. Blanco, C., et al., *Risk factors for anxiety disorders: common and specific effects in a national sample.* Depression and anxiety, 2014. **31**(9): p. 756-764.

9. Zhang, X., et al., *Generalized anxiety in community-dwelling elderly: prevalence and clinical characteristics.* Journal of affective disorders, 2015. **172**: p. 24-29.

10. McLean, C.P., et al., *Gender differences in anxiety disorders: prevalence, course of illness, comorbidity and burden of illness.* Journal of psychiatric research, 2011. **45**(8): p. 1027-1035.

11. APA. *What Are Anxiety Disorders?* 2017; Available from: https://www.psychiatry.org/patients-families/anxiety-disorders/what-are-anxiety-disorders#:~:text=Risk%20Factors,stresses%20can%20produce%20the%20disorders.

12. Lieb, R., et al., *Parental major depression and the risk of depression and other mental disorders in offspring: a prospective-longitudinal community study.* Arch Gen Psychiatry, 2002. **59**(4): p. 365-74.

13. Neckelmann, D., A. Mykletun, and A.A. Dahl, *Chronic insomnia as a risk factor for developing anxiety and depression.* Sleep, 2007. **30**(7): p. 873-880.

14. Nahon, S., et al., *Risk factors of anxiety and depression in inflammatory bowel disease.* Inflamm Bowel Dis, 2012. **18**(11): p. 2086-91.

15. Bienvenu, O.J. and M.B. Stein, *Personality and anxiety disorders: a review.* Journal of Personality disorders, 2003. **17**(2: Special issue): p. 139-151.

16. Norton, G.R., et al., *Personality factors associated with generalized and non-generalized social anxiety.* Personality and Individual Differences, 1997. **22**(5): p. 655-660.

17. Hendriks, S.M., et al., *Disability in anxiety disorders.* Journal of affective disorders, 2014. **166**: p. 227-233.

18. Baxter, A.J., et al., *Challenging the myth of an "epidemic" of common mental disorders: trends in the global prevalence of anxiety and depression between 1990 and 2010.* Depress Anxiety, 2014. **31**(6): p. 506-16.

Copyright ©2021 Reed Group, Ltd.

19. Wittchen, H.U., et al., *The size and burden of mental disorders and other disorders of the brain in Europe 2010.* Eur Neuropsychopharmacol, 2011. **21**(9): p. 655-79.

20. Haro, J.M., et al., *ROAMER: roadmap for mental health research in Europe.* International Journal of Methods in Psychiatric Research, 2014. **23**(S1): p. 1-14.

21. Emdin, C.A., et al., *Meta-analysis of anxiety as a risk factor for cardiovascular disease.* The American journal of cardiology, 2016. **118**(4): p. 511-519.

22. Allgulander, C., *Anxiety as a risk factor in cardiovascular disease.* Current Opinion in Psychiatry, 2016. **29**(1): p. 13-17.

23. Nabi, H., et al., *Psychological and somatic symptoms of anxiety and risk of coronary heart disease: the health and social support prospective cohort study.* Biological psychiatry, 2010. **67**(4): p. 378-385.

24. Albert, C.M., et al., *Phobic anxiety and risk of coronary heart disease and sudden cardiac death among women.* Circulation, 2005. **111**(4): p. 480-7.

25. Kawachi, I., et al., *Prospective study of phobic anxiety and risk of coronary heart disease in men.* Circulation, 1994. **89**(5): p. 1992-7.

26. Kindler, S., et al., *Depressive and anxiety symptoms as risk factors for temporomandibular joint pain: a prospective cohort study in the general population.* The Journal of Pain, 2012. **13**(12): p. 1188-1197.

27. McWilliams, L.A., B.J. Cox, and M.W. Enns, *Mood and anxiety disorders associated with chronic pain: an examination in a nationally representative sample.* Pain, 2003. **106**(1-2): p. 127-33.

28. Spence, M.J. and R. Moss-Morris, *The cognitive behavioural model of irritable bowel syndrome: a prospective investigation of patients with gastroenteritis.* Gut, 2007. **56**(8): p. 1066-71.

29. Buckner, J.D., et al., *Specificity of social anxiety disorder as a risk factor for alcohol and cannabis dependence.* Journal of psychiatric research, 2008. **42**(3): p. 230-239.

30. Moylan, S., et al., *Cigarette smoking, nicotine dependence and anxiety disorders: a systematic review of population-based, epidemiological studies.* BMC Med, 2012. **10**: p. 123.

31. Meier, S.M., et al., *Secondary depression in severe anxiety disorders: a population-based cohort study in Denmark.* Lancet Psychiatry, 2015. **2**(6): p. 515-23.

32. Wittchen, H.U., et al., *Why do people with anxiety disorders become depressed? A prospective-longitudinal community study.* Acta Psychiatr Scand Suppl, 2000(406): p. 14-23.

33. Erickson, S.R., et al., *Severity of anxiety and work-related outcomes of patients with anxiety disorders.* Depress Anxiety, 2009. **26**(12): p. 1165-71.

34. Hendriks, S.M., et al., *Long-term work disability and absenteeism in anxiety and depressive disorders.* Journal of affective disorders, 2015. **178**: p. 121-130.

35. Plaisier, I., et al., *Work functioning in persons with depressive and anxiety disorders: the role of specific psychopathological characteristics.* Journal of affective disorders, 2010. **125**(1-3): p. 198-206.

36. Plaisier, I., et al., *Depressive and anxiety disorders on-the-job: the importance of job characteristics for good work functioning in persons with depressive and anxiety disorders.* Psychiatry research, 2012. **200**(2-3): p. 382-388.

37. American Psychiatric Association, *Diagnostic and statistical manual of mental disorders : DSM-5*. 5th ed. 2013, Washington, D.C.: American Psychiatric Association. xliv, 947 p.

Copyright ©2021 Reed Group, Ltd.

38. Association, A.P., *Diagnostic and statistical manual of mental disorders : DSM-IV : international version with ICD-10 codes*. 4th ed. 1995, Washington, D.C.: American Psychiatric Association. xxvii, 900 p.

39. American Psychiatric Association, *Diagnostic and statistical manual of mental disorders : DSM-IV-TR*. 4th ed. 2000, Washington, DC: American Psychiatric Association. xxxvii, 943 p.

40. World Health Organization. *The International Classification of Diseases 11th Revision*. 2019 [cited 2019 March 6]; Available from: https://icd.who.int/en.

41. World Health Organization. *International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM)*. 2010 [cited 2010 November, 5]; Available from: http://www.cdc.gov/nchs/icd/icd10cm.htm.

42. Willers, L.E., et al., *The origin of anxiety disorders - an evolutionary approach.* Mod Trends Pharmacopsychiatry, 2013. **29**: p. 16-23.

43. Bateson, M., B. Brilot, and D. Nettle, *Anxiety: an evolutionary approach.* Can J Psychiatry, 2011. **56**(12): p. 707-15.

44. Tovote, P., J.P. Fadok, and A. Luthi, *Neuronal circuits for fear and anxiety.* Nat Rev Neurosci, 2015. **16**(6): p. 317-31.

45. Brosschot, J.F., B. Verkuil, and J.F. Thayer, *The default response to uncertainty and the importance of perceived safety in anxiety and stress: An evolution-theoretical perspective.* Journal of Anxiety Disorders, 2016. **41**: p. 22-34.

46. Gross, C. and R. Hen, *The developmental origins of anxiety.* Nature Reviews Neuroscience, 2004. **5**(7): p. 545-552.

47. Waters, A.M. and M.G. Craske, *Towards a cognitive-learning formulation of youth anxiety: A narrative review of theory and evidence and implications for treatment.* Clinical Psychology Review, 2016. **50**: p. 50-66.

48. Cannon WB, *Bodily changes in pain, hunger, fear, and rage*. 1929, New York: Appleton-Century.

49. Vrinten, C., et al., *What do people fear about cancer? A systematic review and meta-synthesis of cancer fears in the general population.* Psychooncology, 2017. **26**(8): p. 1070-1079.

50. Selye, H., *Stress in health and disease*. 1976, Boston: Butterworths. xliii, 1256 p.

51. Selye, H., *A personal message from Hans Selye.* Journal of Extension, 1980. **18**(3 May/June): p. 6-11.

52. Porges, S.W., *The polyvagal theory: new insights into adaptive reactions of the autonomic nervous system.* Cleve Clin J Med, 2009. **76 Suppl 2**: p. S86-90.

53. Porges, S.W., *The polyvagal perspective.* Biol Psychol, 2007. **74**(2): p. 116-43.

54. Jackson, J.H., *Selected writings of John Hughlings Jackson*. Vol. 1. 1958: Staples.

55. Porges, S.W., *The Polyvagal Theory: phylogenetic contributions to social behavior.* Physiol Behav, 2003. **79**(3): p. 503-13.

56. Porges, S.W., *The polyvagal theory: phylogenetic substrates of a social nervous system.* Int J Psychophysiol, 2001. **42**(2): p. 123-46.

57. Porges, S.W., *The pocket guide to the polyvagal theory : the transformative power of feeling safe*. First edition. ed. The Norton series on interpersonal neurobiology. 2017, New York: W. W Norton & Company. xvi, 254 pages.

58. Porges, S.W., *The polyvagal theory : neurophysiological foundations of emotions, attachment, communication, and self-regulation*. 1st ed. The Norton series on interpersonal neurobiology. 2011, New York: W. W. Norton. xvii, 347 p.

59. Porges, S.W. and D. Dana, *Clinical applications of the polyvagal theory : the emergence of polyvagal-informed therapies*. First edition. ed. Norton series on interpersonal neurobiology. 2018, New York: W.W. Norton & Company. p.

Copyright ©2021 Reed Group, Ltd.

60. Stahl, S.M., *Stahl's essential psychopharmacology : neuroscientific basis and practical application*. 4th ed. 2013, Cambridge ; New York: Cambridge University Press. xv, 608 p.

61. Misiewicz, Z., et al., *Multi-omics analysis identifies mitochondrial pathways associated with anxiety-related behavior.* PLoS genetics, 2019. **15**(9): p. e1008358.

62. Fox, A.S., et al., *Functional Connectivity within the Primate Extended Amygdala Is Heritable and Associated with Early-Life Anxious Temperament.* J Neurosci, 2018. **38**(35): p. 7611-7621.

63. Knight, L.K. and B.E. Depue, *New frontiers in anxiety research: The translational potential of the bed nucleus of the stria terminalis.* Frontiers in psychiatry, 2019. **10**: p. 510.

64. Makovac, E., et al., *Network abnormalities in generalized anxiety pervade beyond the amygdala-pre-frontal cortex circuit: Insights from graph theory.* Psychiatry Res Neuroimaging, 2018. **281**: p. 107-116.

65. Klumpp, H. and J.M. Fitzgerald, *Neuroimaging Predictors and Mechanisms of Treatment Response in Social Anxiety Disorder: an Overview of the Amygdala.* Curr Psychiatry Rep, 2018. **20**(10): p. 89.

66. Brandao, M.L. and N.C. Coimbra, *Understanding the role of dopamine in conditioned and unconditioned fear.* Rev Neurosci, 2019. **30**(3): p. 325-337.

67. Kneer, K., et al., *Serotonergic influence on depressive symptoms and trait anxiety is mediated by negative life events and frontal activation in children and adolescents.* Eur Child Adolesc Psychiatry, 2020. **29**(5): p. 691-706.

68. Kalueff, A.V. and D.J. Nutt, *Role of GABA in anxiety and depression.* Depress Anxiety, 2007. **24**(7): p. 495-517.

69. Zorumski, C.F., et al., *Neurosteroids as novel antidepressants and anxiolytics: GABA-A receptors and beyond.* Neurobiol Stress, 2019. **11**: p. 100196.

70. Yohn, C.N., M.M. Gergues, and B.A. Samuels, *The role of 5-HT receptors in depression.* Molecular brain, 2017. **10**(1): p. 1-12.

71. Montoya, A., et al., *The noradrenergic paradox: implications in the management of depression and anxiety.* Neuropsychiatr Dis Treat, 2016. **12**: p. 541-57.

72. Bulley, A., et al., *An evolutionary perspective on the co-occurrence of social anxiety disorder and alcohol use disorder.* J Affect Disord, 2016. **196**: p. 62-70.

73. Torres, N., *Testing a Neuro-Evolutionary Theory of Social Bonds and Addiction: Methadone Associated With Lower Attachment Anxiety, Comfort With Closeness, and Proximity Maintenance.* Front Psychiatry, 2019. **10**: p. 602.

74. Cloninger, C.R., *A unified biosocial theory of personality and its role in the development of anxiety states.* Psychiatr Dev, 1986. **4**(3): p. 167-226.

75. Beck, A.T., *A 60-Year Evolution of Cognitive Theory and Therapy.* Perspectives on Psychological Science, 2019. **14**(1): p. 16-20.

76. Behar, E., et al., *Current theoretical models of generalized anxiety disorder (GAD): conceptual review and treatment implications.* J Anxiety Disord, 2009. **23**(8): p. 1011-23.

77. American Psychological Association, *APA Dictionary of Clinical Psychology*. 2012, Washington, DC: American Psychological Association.

78. Beck, A.T., *The current state of cognitive therapy: a 40-year retrospective.* Arch Gen Psychiatry, 2005. **62**(9): p. 953-9.

79. Piaget, J. and M. Cook, *The origins of intelligence in children*. Vol. 8. 1952: International Universities Press New York.

Copyright ©2021 Reed Group, Ltd.

80. Kelly, G., G.A. Kelly, and G.A. Kelly, *A theory of personality: The psychology of personal constructs*. 1963: WW Norton & Company.

81. Beck, A.T. and A.J. Rush, *A cognitive model of anxiety formation and anxiety resolution.* Issues Ment Health Nurs, 1985. **7**(1-4): p. 349-65.

82. Wood, T.J., et al., *Preoperative Predictors of Pain Catastrophizing, Anxiety, and Depression in Patients Undergoing Total Joint Arthroplasty.* J Arthroplasty, 2016.

83. Weiss, K.E., et al., *Acceptance of pain: associations with depression, catastrophizing, and functional disability among children and adolescents in an interdisciplinary chronic pain rehabilitation program.* J Pediatr Psychol, 2013. **38**(7): p. 756-65.

84. Velly, A.M., et al., *The effect of catastrophizing and depression on chronic pain--a prospective cohort study of temporomandibular muscle and joint pain disorders.* Pain, 2011. **152**(10): p. 2377-83.

85. Linton, S.J., et al., *The role of depression and catastrophizing in musculoskeletal pain.* Eur J Pain, 2011. **15**(4): p. 416-22.

86. Edwards, R.R., et al., *Pain, catastrophizing, and depression in the rheumatic diseases.* Nat Rev Rheumatol, 2011. **7**(4): p. 216-24.

87. Trocoli, T.O. and R.V. Botelho, *Prevalence of anxiety, depression and kinesiophobia in patients with low back pain and their association with the symptoms of low back spinal pain.* Rev Bras Reumatol Engl Ed, 2016. **56**(4): p. 330-6.

88. Oskay, D., et al., *Relationship between kinesiophobia and pain, quality of life, functional status, disease activity, mobility, and depression in patients with ankylosing spondylitis.* Turk J Med Sci, 2017. **47**(5): p. 1340-1347.

89. Filardo, G., et al., *Kinesiophobia and depression affect total knee arthroplasty outcome in a multivariate analysis of psychological and physical factors on 200 patients.* Knee Surg Sports Traumatol Arthrosc, 2017. **25**(11): p. 3417-3423.

90. Beck, A.T., *Thinking and Depression. II. Theory and Therapy.* Arch Gen Psychiatry, 1964 **10**: p. 561-71.

91. Seligman, M.E., *Learned optimism.* 1991, New York: Knopf.

92. Thorn, B.E., et al., *Literacy-Adapted Cognitive Behavioral Therapy Versus Education for Chronic Pain at Low-Income Clinics: A Randomized Controlled Trial.* Ann Intern Med, 2018. **168**(7): p. 471-480.

93. Miller, W.R., M.E. Seligman, and H.M. Kurlander, *Learned helplessness, depression, and anxiety.* J Nerv Ment Dis, 1975. **161**(5): p. 347-57.

94. Maier, S.F. and M.E.P. Seligman, *Learned helplessness at fifty: Insights from neuroscience.* Psychological review, 2016. **123**(4): p. 349-367.

95. Beck, A.T., *Cognitive Therapy: Nature and Relation to Behavior Therapy - Republished Article.* Behav Ther, 2016. **47**(6): p. 776-784.

96. Abramowitz, J.S., *The practice of exposure therapy: relevance of cognitive-behavioral theory and extinction theory.* Behav Ther, 2013. **44**(4): p. 548-58.

97. Ougrin, D., *Efficacy of exposure versus cognitive therapy in anxiety disorders: systematic review and meta-analysis.* BMC Psychiatry, 2011. **11**(1): p. 200.

98. Clark, D.A. and A.T. Beck, *Cognitive theory and therapy of anxiety and depression: convergence with neurobiological findings.* Trends Cogn Sci, 2010. **14**(9): p. 418-24.

99. Beck, A.T., *The evolution of the cognitive model of depression and its neurobiological correlates.* Am J Psychiatry, 2008. **165**(8): p. 969-77.

Copyright ©2021 Reed Group, Ltd.

100. Franklin, G., A.J. Carson, and K.A. Welch, *Cognitive behavioural therapy for depression: systematic review of imaging studies.* Acta Neuropsychiatr, 2016. **28**(2): p. 61-74.

101. Williams, N., *AMA Guides to the Evaluation of Work Ability and Return to Work.* Occupational Medicine, 2012. **62**(2): p. 155-155.

102. Arends, I., J.J. van der Klink, and U. Bültmann, *Prevention of recurrent sickness absence among employees with common mental disorders: design of a cluster-randomised controlled trial with cost-benefit and effectiveness evaluation.* BMC public health, 2010. **10**(1): p. 1-9.

103. Barsky, A. and S.A. Kaplan, *If you feel bad, it's unfair: A quantitative synthesis of affect and organizational justice perceptions.* Journal of applied psychology, 2007. **92**(1): p. 286.

104. Nilsson, G.H., et al., *Psychiatrists' work with sickness certification: frequency, experiences and severity of the certification tasks in a national survey in Sweden.* BMC health services research, 2012. **12**(1): p. 362.

105. Smith, P.M., et al., *Are the predictors of work absence following a work-related injury similar for musculoskeletal and mental health claims?* Journal of occupational rehabilitation, 2013. **24**(1): p. 79-88.

106. Modini, M., et al., *The mental health benefits of employment: Results of a systematic meta-review.* Australasian Psychiatry, 2016. **24**(4): p. 331-336.

107. Barsky, A.J., *Forgetting, fabricating, and telescoping: the instability of the medical history.* Archives of internal medicine, 2002. **162**(9): p. 981-984.

108. Barsky, A.J., *The iatrogenic potential of the physician's words.* Jama, 2017. **318**(24): p. 2425-2426.

109. Colloca, L. and A.J. Barsky, *Placebo and nocebo effects.* New England Journal of Medicine, 2020. **382**(6): p. 554-561.

110. Engblom, M., et al., *Frequency and severity of problems that general practitioners experience regarding sickness certification.* Scandinavian journal of primary health care, 2011. **29**(4): p. 227-233.

111. Harding, T.P., *Psychiatric disability and clinical decision making: The impact of judgment error and bias.* Clinical Psychology Review, 2004. **24**(6): p. 707-729.

112. Kiessling, A., et al., *Quality of medical certificates issued in long-term sick leave or disability in relation to patient characteristics and delivery of health care.* Scandinavian journal of public health, 2013. **41**(4): p. 412-420.

113. Løvvik, C., et al., *Association between illness perceptions and return-to-work expectations in workers with common mental health symptoms.* Journal of occupational rehabilitation, 2013. **24**(1): p. 160-170.

114. Nilsing, E., et al., *Description of functioning in sickness certificates.* Scandinavian journal of public health, 2011. **39**(5): p. 508-516.

115. Nilsing, E., E. Söderberg, and B. Öberg, *Sickness certificates in Sweden: did the new guidelines improve their quality?* BMC public health, 2012. **12**(1): p. 907.

116. Reicherts, P., et al., *Psychological placebo and nocebo effects on pain rely on expectation and previous experience.* The Journal of Pain, 2016. **17**(2): p. 203-214.

117. Warren, P.A., *Behavioral health disability: Innovations in prevention and management*. 2010: Springer Science & Business Media.

118. Warren, P.A., *Handbook of behavioral health disability management*. 2018: Springer.

119. Nyberg, J., et al., *Effects of exercise on symptoms of anxiety, cognitive ability and sick leave in patients with anxiety disorders in primary care: study protocol for PHYSBI, a randomized controlled trial.* BMC psychiatry, 2019. **19**(1): p. 172.

Copyright ©2021 Reed Group, Ltd.

120. O'Donnell, M.L., et al., *A systematic review of psychological and pharmacological treatments for adjustment disorder in adults.* Journal of traumatic stress, 2018. **31**(3): p. 321-331.

121. Overbeck, G., A.S. Davidsen, and M.B. Kousgaard, *Enablers and barriers to implementing collaborative care for anxiety and depression: a systematic qualitative review.* Implementation Science, 2016. **11**(1): p. 165.

122. Boisseau, C.L. and S.L. Garnaat, *Introduction to the Special Issue on Cognitive and Behavioral Flexibility in Fear and Anxiety Disorders*. 2018, SAGE Publications Sage CA: Los Angeles, CA.

123. Cisler, J.M. and B.O. Olatunji, *Emotion regulation and anxiety disorders.* Current psychiatry reports, 2012. **14**(3): p. 182-187.

124. Hofmann, S.G. and A.C. Hay, *Rethinking avoidance: Toward a balanced approach to avoidance in treating anxiety disorders.* Journal of anxiety disorders, 2018. **55**: p. 14-21.

125. Kneeland, E.T., et al., *Emotion malleability beliefs, emotion regulation, and psychopathology: Integrating affective and clinical science.* Clinical psychology review, 2016. **45**: p. 81-88.

126. Kneeland, E.T., F.R. Goodman, and J.F. Dovidio, *Emotion beliefs, emotion regulation, and emotional experiences in daily life.* Behavior Therapy, 2020. **51**(5): p. 728-738.

127. LeDoux, J.E., et al., *The birth, death and resurrection of avoidance: a reconceptualization of a troubled paradigm.* Molecular psychiatry, 2017. **22**(1): p. 24-36.

128. Morriss, J., A. Christakou, and C.M. Van Reekum, *Intolerance of uncertainty predicts fear extinction in amygdala-ventromedial prefrontal cortical circuitry.* Biology of mood & anxiety disorders, 2015. **5**(1): p. 1-13.

129. Gaspar, F.W., C.S. Zaidel, and C.S. Dewa, *Rates and predictors of recurrent work disability due to common mental health disorders in the United States.* PloS one, 2018. **13**(10): p. e0205170.

130. Gjesdal, S., et al., *GP consultations for common mental disorders and subsequent sickness certification: register-based study of the employed population in Norway.* Family Practice, 2016. **33**(6): p. 656-662.

131. González-Blanch, C., et al., *Domain-specific associations between disability and depression, anxiety, and somatization in primary care patients.* Psychiatry Research, 2018. **269**: p. 596-601.

132. Sawchuk, C.N., et al., *Initial outcomes of a real-world multi-site primary care psychotherapy program.* General hospital psychiatry, 2018. **54**: p. 5-11.

133. Shafran, R., et al., *Cognitive behaviour treatment of co-occurring depression and generalised anxiety in routine clinical practice.* PloS one, 2018. **13**(7): p. e0201226.

134. Palm Reed, K.M., A.Y. Cameron, and V.E. Ameral, *A contextual behavior science framework for understanding how behavioral flexibility relates to anxiety.* Behavior modification, 2018. **42**(6): p. 914-931.

135. Tempesta, D., et al., *Neuropsychological functioning in young subjects with generalized anxiety disorder with and without pharmacotherapy.* Progress in Neuro-Psychopharmacology and Biological Psychiatry, 2013. **45**: p. 236-241.

136. Fujii, Y., et al., *Severity of generalized social anxiety disorder correlates with low executive functioning.* Neuroscience letters, 2013. **543**: p. 42-46.

137. Zainal, N.H. and M.G. Newman, *Executive function and other cognitive deficits are distal risk factors of generalized anxiety disorder 9 years later.* Psychological medicine, 2018. **48**(12): p. 2045.

138. Goldstein, J.M., et al., *Sex differences in stress response circuitry activation dependent on female hormonal cycle.* Journal of Neuroscience, 2010. **30**(2): p. 431-438.

Copyright ©2021 Reed Group, Ltd.

139. Kogler, L., R.C. Gur, and B. Derntl, *Sex differences in cognitive regulation of psychosocial achievement stress: brain and behavior.* Human brain mapping, 2015. **36**(3): p. 1028-1042.

140. Milad, M.R., et al., *Fear conditioning and extinction: influence of sex and menstrual cycle in healthy humans.* Behavioral neuroscience, 2006. **120**(6): p. 1196.

141. Kelly, M.M. and J.P. Forsyth, *Sex differences in response to an observational fear conditioning procedure.* Behavior therapy, 2007. **38**(4): p. 340-349.

142. Antov, M.I. and U. Stockhorst, *Stress exposure prior to fear acquisition interacts with estradiol status to alter recall of fear extinction in humans.* Psychoneuroendocrinology, 2014. **49**: p. 106-118.

143. Baran, S.E., et al., *Chronic stress and sex differences on the recall of fear conditioning and extinction.* Neurobiology of learning and memory, 2009. **91**(3): p. 323-332.

144. Bentz, D., et al., *Influence of stress on fear memory processes in an aversive differential conditioning paradigm in humans.* Psychoneuroendocrinology, 2013. **38**(7): p. 1186-1197.

145. Graham, B.M., C. Ash, and M.L. Den, *High endogenous estradiol is associated with enhanced cognitive emotion regulation of physiological conditioned fear responses in women.* Psychoneuroendocrinology, 2017. **80**: p. 7-14.

146. Altemus, M., N. Sarvaiya, and C.N. Epperson, *Sex differences in anxiety and depression clinical perspectives.* Frontiers in neuroendocrinology, 2014. **35**(3): p. 320-330.

147. Merz, C.J., et al., *Neuronal correlates of extinction learning are modulated by sex hormones.* Social Cognitive and Affective Neuroscience, 2012. **7**(7): p. 819-830.

148. Merz, C.J., et al., *Stress differentially affects fear conditioning in men and women.* Psychoneuroendocrinology, 2013. **38**(11): p. 2529-2541.

149. Stark, R., et al., *Influence of the stress hormone cortisol on fear conditioning in humans: evidence for sex differences in the response of the prefrontal cortex.* Neuroimage, 2006. **32**(3): p. 1290-1298.

150. Zorawski, M., et al., *Effects of stress and sex on acquisition and consolidation of human fear conditioning.* Learning & memory, 2006. **13**(4): p. 441-450.

151. Zorawski, M., et al., *Sex, stress, and fear: individual differences in conditioned learning.* Cognitive, Affective, & Behavioral Neuroscience, 2005. **5**(2): p. 191-201.

152. Hickey, M., C. Bryant, and F. Judd, *Evaluation and management of depressive and anxiety symptoms in midlife.* Climacteric, 2012. **15**(1): p. 3-9.

153. Maeng, L.Y., J. Waddell, and T.J. Shors, *The prefrontal cortex communicates with the amygdala to impair learning after acute stress in females but not in males.* Journal of Neuroscience, 2010. **30**(48): p. 16188-16196.

154. Maeng, L.Y. and T.J. Shors, *The stressed female brain: neuronal activity in the prelimbic but not infralimbic region of the medial prefrontal cortex suppresses learning after acute stress.* Frontiers in neural circuits, 2013. **7**: p. 198.

155. Van Veen, J.F., et al., *The effects of female reproductive hormones in generalized social anxiety disorder.* The International Journal of Psychiatry in Medicine, 2009. **39**(3): p. 283-295.

156. Cover, K., et al., *Mechanisms of estradiol in fear circuitry: implications for sex differences in psychopathology.* Translational psychiatry, 2014. **4**(8): p. e422-e422.

157. Katzman, M.A., et al., *Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive-compulsive disorders.* BMC psychiatry, 2014. **14**(S1): p. S1.

Copyright ©2021 Reed Group, Ltd.

158. Li, S.H. and B.M. Graham, *Why are women so vulnerable to anxiety, trauma-related and stress-related disorders? The potential role of sex hormones.* The Lancet Psychiatry, 2017. **4**(1): p. 73-82.

159. Poulin, L.E., et al., *The predictive capacity of self-reported motivation vs. early observed motivational language in cognitive behavioural therapy for generalized anxiety disorder.* Cognitive behaviour therapy, 2019. **48**(5): p. 369-384.

160. Rothermund, E., et al., *Improving access to mental health care by delivering psychotherapeutic care in the workplace: a cross-sectional exploratory trial.* PloS one, 2017. **12**(1): p. e0169559.

161. Rivière, M., et al., *Management of work-related common mental disorders in general practice: a cross-sectional study.* BMC Family Practice, 2020. **21**(1): p. 1-9.

162. Hall, K.A.A., et al., *The impact bias in self and others: Affective and empathic forecasting in individuals with social anxiety.* Behaviour research and therapy, 2018. **106**: p. 37-46.

163. Carpenter, J.K., M. Pinaire, and S.G. Hofmann, *from extinction learning to anxiety treatment: Mind the gap.* Brain sciences, 2019. **9**(7): p. 164.

164. Dymond, S., *Overcoming avoidance in anxiety disorders: The contributions of Pavlovian and operant avoidance extinction methods.* Neuroscience & Biobehavioral Reviews, 2019. **98**: p. 61-70.

165. Chamoux, A., et al., *Occupational exposure factors for mental and behavioral disorders at work: The FOREC thesaurus.* PloS one, 2018. **13**(6): p. e0198719.

166. Harvey, S.B., et al., *Can work make you mentally ill? A systematic meta-review of work-related risk factors for common mental health problems.* Occupational and environmental medicine, 2017. **74**(4): p. 301-310.

167. da Silva-Junior, J.S. and F.M. Fischer, *Long-term sickness absence due to mental disorders is associated with individual features and psychosocial work conditions.* PLoS One, 2014. **9**(12): p. e115885.

168. Nieuwenhuijsen, K., D. Bruinvels, and M. Frings-Dresen, *Psychosocial work environment and stress-related disorders, a systematic review.* Occupational medicine, 2010. **60**(4): p. 277-286.

169. Roelen, C.A., et al., *Sickness absence and psychosocial work conditions: a multilevel study.* Occupational medicine, 2008. **58**(6): p. 425-430.

170. Hinkka, K., et al., *Psychosocial work factors and sick leave, occupational accident, and disability pension: a cohort study of civil servants.* Journal of occupational and environmental medicine, 2013. **55**(2): p. 191-197.

171. Karlsson, N.E., et al., *Risk factors for disability pension in a population-based cohort of men and women on long-term sick leave in Sweden.* European journal of public health, 2008. **18**(3): p. 224-231.

172. Ropponen, A., et al., *Personality traits and life dissatisfaction as risk factors for disability pension due to low back diagnoses: A 30-year longitudinal cohort study of Finnish twins.* Journal of psychosomatic research, 2012. **73**(4): p. 289-294.

173. Samuelsson, Å., et al., *A prospective cohort study of disability pension due to mental diagnoses: the importance of health factors and behaviors.* BMC Public Health, 2013. **13**(1): p. 621.

174. Samuelsson, Å., et al., *Psychosocial working conditions, occupational groups, and risk of disability pension due to mental diagnoses: a cohort study of 43 000 Swedish twins.* Scandinavian journal of work, environment & health, 2013: p. 351-360.

175. Bailey, S.K., J. Haggarty, and S. Kelly, *Global absenteeism and presenteeism in mental health patients referred through primary care.* Work, 2016. **53**(2): p. 399-408.

Copyright ©2021 Reed Group, Ltd.

176. Bergström, G., et al., *Preventing sickness absenteeism among employees with common mental disorders or stress-related symptoms at work: Design of a cluster randomized controlled trial of a problem-solving based intervention versus care-as-usual conducted at the Occupational Health Services.* BMC Public Health, 2017. **17**(1): p. 1-10.

177. Hofmann, B., *Medicalization and overdiagnosis: different but alike.* Medicine, Health Care and Philosophy, 2016. **19**(2): p. 253-264.

178. Stolper, E., et al., *Gut feelings as a third track in general practitioners' diagnostic reasoning.* Journal of general internal medicine, 2011. **26**(2): p. 197-203.

179. Vaez, M., et al., *Sickness absence and disability pension in a cohort of employees initially on long-term sick leave due to psychiatric disorders in Sweden.* Social psychiatry and psychiatric epidemiology, 2007. **42**(5): p. 381-388.

180. Wakefield, J.C., *Misdiagnosing normality: Psychiatry's failure to address the problem of false positive diagnoses of mental disorder in a changing professional environment.* Journal of Mental Health, 2010. **19**(4): p. 337-351.

181. Wallman, T., et al., *Sick-leave track record and other potential predictors of a disability pension. A population based study of 8,218 men and women followed for 16 years.* BMC Public Health, 2009. **9**(1): p. 104.

182. Bokma, W.A., et al., *Impact of Anxiety and/or Depressive Disorders and Chronic Somatic Diseases on disability and work impairment.* Journal of psychosomatic research, 2017. **94**: p. 10-16.

183. Gaspar, F.W., et al., *Pre-existing and new-onset depression and anxiety among workers with injury or illness work leaves.* Journal of occupational and environmental medicine, 2020. **62**(10): p. e567.

184. Theis, K.A., et al., *Prevalence and causes of work disability among working-age US adults, 2011–2013, NHIS.* Disability and health journal, 2018. **11**(1): p. 108-115.

185. Torquati, L., et al., *Shift work and poor mental health: A meta-analysis of longitudinal studies.* American journal of public health, 2019. **109**(11): p. e13-e20.

186. Vignoli, M., B. Muschalla, and M.G. Mariani, *Workplace phobic anxiety as a mental health phenomenon in the job demands-resources model.* BioMed research international, 2017. **2017**.

187. Thun, E., et al., *Unravelling the Prospective Associations Between Mixed Anxiety-Depression and Insomnia During the Course of Cognitive Behavioral Therapy.* Psychosomatic medicine, 2019. **81**(4): p. 333-340.

188. Roma, P., et al., *Psychopathological characteristics of adjustment disorder among outpatients with and without work related stress.* Giornale italiano di medicina del lavoro ed ergonomia, 2017. **39**(2): p. 72-77.

189. Bonham, C.A. and E. Uhlenhuth, *Disability and comorbidity: diagnoses and symptoms associated with disability in a clinical population with panic disorder.* Psychiatry journal, 2014. **2014**.

190. Brown, L.A., et al., *Does CBT for anxiety-related disorders alter suicidal ideation? Findings from a naturalistic sample.* Journal of anxiety disorders, 2018. **59**: p. 10-16.

191. Buselli, R., et al., *Mental disability management within occupational health surveillance.* La Medicina Del Lavoro, 2020. **111**(3): p. 232-240.

192. Campbell-Sills, L., et al., *Improving outcomes for patients with medication-resistant anxiety: effects of collaborative care with cognitive behavioral therapy.* Depression and Anxiety, 2016. **33**(12): p. 1099-1106.

193. Covell, C.L., et al., *Mapping the peer-reviewed literature on accommodating nurses' return to work after leaves of absence for mental health issues: a scoping review.* Human resources for health, 2020. **18**(1): p. 1-7.

194. Muschalla, B., *Work-anxiety rather than cognitive performance contributes to workability decisions in patients with mental disorders.* Journal of Occupational and Environmental Medicine, 2018. **60**(11): p. 1042-1048.

Copyright ©2021 Reed Group, Ltd.

195. Muschalla, B. and M. Jöbges, *Prevalence and Characteristics of Work Anxiety in Medical Rehabilitation Patients: A Cross-Sectional Observation Study.* Archives of physical medicine and rehabilitation, 2018. **99**(1): p. 57-64.

196. Muschalla, B., B. Flöge, and M. Linden, *UNWANTED EFFECTS WITHIN A COGNITIVE BEHAVIORAL THERAPY GROUP IN COMPARISON WITH A RECREATIONAL GROUP-A CLUSTER RANDOMIZED CONTROLLED TRIAL.* Psychiatria Danubina, 2020. **32**(1): p. 115-121.

197. Muschalla, B., et al., *Mental health problem or workplace problem or something else: what contributes to work perception?* Disability and Rehabilitation, 2020. **42**(4): p. 502-509.

198. von Brachel, R., et al., *Long-term effectiveness of cognitive behavioral therapy in routine outpatient care: a 5-to 20-year follow-up study.* Psychotherapy and psychosomatics, 2019. **88**(4): p. 225-235.

199. Curran, H.V., *Tranquillising memories: A review of the effects of benzodiazepines on human memory.* Biological Psychology, 1986. **23**(2): p. 179-213.

200. Valerie Curran, H., *Benzodiazepines, memory and mood: a review.* Psychopharmacology, 1991. **105**(1): p. 1-8.

201. Buffett-Jerrott, S.E. and S.H. Stewart, *Cognitive and Sedative Effects of Benzodiazepine Use.* Current Pharmaceutical Design, 2002. **8**(1): p. 45-58.

202. Thomas, R.E., *Benzodiazepine use and motor vehicle accidents. Systematic review of reported association.* Canadian family physician Medecin de famille canadien, 1998. **44**: p. 799-808.

203. Bunn, T., M. Singleton, and I.C. Chen, *Use of multiple data sources to identify specific drugs and other factors associated with drug and alcohol screening of fatally injured motor vehicle drivers.* Accident Analysis & Prevention, 2019. **122**: p. 287-294.

204. Penninkilampi, R. and G.D. Eslick, *A Systematic Review and Meta-Analysis of the Risk of Dementia Associated with Benzodiazepine Use, After Controlling for Protopathic Bias.* CNS Drugs, 2018. **32**(6): p. 485-497.

205. Díaz-Gutiérrez, M.J., et al., *Relationship between the use of benzodiazepines and falls in older adults: A systematic review.* Maturitas, 2017. **101**: p. 17-22.

206. Park, H., et al., *Medications associated with falls in older people: systematic review of publications from a recent 5-year period.* European Journal of Clinical Pharmacology, 2015. **71**(12): p. 1429-1440.

207. Narusyte, J., et al., *Shared liability to pain, common mental disorders, and long-term work disability differs among women and men.* Pain, 2020. **161**(5): p. 1005.

208. Nelson, H.D., et al., *Screening for anxiety in adolescent and adult women: a systematic review for the Women's Preventive Services Initiative.* Annals of Internal Medicine, 2020.

209. Salomonsson, S., E. Hedman-Lagerlöf, and L.-G. Öst, *Sickness absence: a systematic review and meta-analysis of psychological treatments for individuals on sick leave due to common mental disorders.* Psychological medicine, 2018. **48**(12): p. 1954-1965.

210. Klumpp, H., et al., *Predicting cognitive behavioral therapy response in social anxiety disorder with anterior cingulate cortex and amygdala during emotion regulation.* NeuroImage: Clinical, 2017. **15**: p. 25-34.

211. Klumpp, H., et al., *Emotion regulation related neural predictors of cognitive behavioral therapy response in social anxiety disorder.* Progress in Neuro-Psychopharmacology and Biological Psychiatry, 2017. **75**: p. 106-112.

212. Niles, A.N., et al., *Applying a novel statistical method to advance the personalized treatment of anxiety disorders: A composite moderator of comparative drop-out from CBT and ACT.* Behaviour Research and Therapy, 2017. **91**: p. 13-23.

Copyright ©2021 Reed Group, Ltd.

213. Nishikawa, Y., et al., *Social anxiety and fear of causing discomfort to others: Diagnostic specificity, symptom correlates and CBT treatment outcome.* Behavioural and Cognitive Psychotherapy, 2017. **45**(4): p. 382.

214. Rubel, J.A., D. Rosenbaum, and W. Lutz, *Patients' in-session experiences and symptom change: Session-to-session effects on a within-and between-patient level.* Behaviour Research and Therapy, 2017. **90**: p. 58-66.

215. Talkovsky, A.M. and P.J. Norton, *Intolerance of uncertainty and transdiagnostic group cognitive behavioral therapy for anxiety.* Journal of anxiety disorders, 2016. **41**: p. 108-114.

216. Zhu, S., et al., *Health-related behaviours and mental health in Hong Kong employees.* Occupational Medicine, 2017. **67**(1): p. 26-32.

217. Langarita-Llorente, R. and P. Gracia-García, *Neuropsicología del trastorno de ansiedad generalizada: revisión sistemática.* Rev. neurol.(Ed. impr.), 2019: p. 59-67.

218. Magaard, J.L., H. Schulz, and A.L. Brütt, *What do patients think about the cause of their mental disorder? A qualitative and quantitative analysis of causal beliefs of mental disorder in inpatients in psychosomatic rehabilitation.* PloS one, 2017. **12**(1): p. e0169387.

219. Ashdown-Franks, G., et al., *Exercise as medicine for mental and substance use disorders: a meta-review of the benefits for neuropsychiatric and cognitive outcomes.* Sports Medicine, 2020: p. 1-20.

220. Firth, J., et al., *A meta-review of "lifestyle psychiatry": the role of exercise, smoking, diet and sleep in the prevention and treatment of mental disorders.* World Psychiatry, 2020. **19**(3): p. 360-380.

221. Lederman, O., et al., *Does exercise improve sleep quality in individuals with mental illness? A systematic review and meta-analysis.* Journal of psychiatric research, 2019. **109**: p. 96-106.

222. McDowell, C.P., et al., *Physical activity and generalized anxiety disorder: results from The Irish Longitudinal Study on Ageing (TILDA).* International Journal of Epidemiology, 2018. **47**(5): p. 1443-1453.

223. Zschucke, E., K. Gaudlitz, and A. Ströhle, *Exercise and physical activity in mental disorders: clinical and experimental evidence.* Journal of Preventive Medicine and Public Health, 2013. **46**(Suppl 1): p. S12.

224. Dias, B.G., et al., *Towards new approaches to disorders of fear and anxiety.* Current opinion in neurobiology, 2013. **23**(3): p. 346-352.

225. ten Have, M., et al., *Insomnia among current and remitted common mental disorders and the association with role functioning: results from a general population study.* Sleep medicine, 2016. **25**: p. 34-41.

226. Thakur, V.K., et al., *An evaluation of large group cognitive behaviour therapy with mindfulness (CBTm) classes.* BMC psychiatry, 2019. **19**(1): p. 132.

227. Johnson, S.U., et al., *Metacognitive therapy versus disorder-specific CBT for comorbid anxiety disorders: a randomized controlled trial.* Journal of anxiety disorders, 2017. **50**: p. 103-112.

228. Johnson, S.U., et al., *Metacognition and cognition in inpatient MCT and CBT for comorbid anxiety disorders: A study of within-person effects.* Journal of counseling psychology, 2018. **65**(1): p. 86.

229. Johnson, S.U. and A. Hoffart, *Moderators and predictors of outcome in metacognitive and cognitive behavioural therapy for co-morbid anxiety disorders.* Clinical psychology & psychotherapy, 2019. **26**(4): p. 399-408.

230. Jothi, N. and W. Husain, *Predicting generalized anxiety disorder among women using Shapley value*. Journal of Infection and Public Health, 2020.

231. Laposa, J.M. and K. Fracalanza, *Does intolerance of uncertainty mediate improvement in anger during group CBT for GAD? A preliminary investigation.* Behavioural and cognitive psychotherapy, 2019. **47**(5): p. 585-593.

Copyright ©2021 Reed Group, Ltd.

232. Lim, J.-A., et al., *Investigating effective treatment factors in brief cognitive behavioral therapy for panic disorder.* Medicine, 2018. **97**(38).

233. Muschalla, B., *Work-Anxieties and their Treatment in Medical Rehabilitation-Hand Tools for Capacity Training and Psychotherapy.* Die Rehabilitation, 2017. **56**(1): p. 38-46.

234. Ritzert, T.R., et al., *Evaluating ACT processes in relation to outcome in self-help treatment for anxiety-related problems.* Behavior modification, 2020. **44**(6): p. 865-890.

235. Rivière, M., et al., *Which work-related characteristics are most strongly associated with common mental disorders? A cross-sectional study.* BMJ open, 2018. **8**(8): p. e020770.

236. Kimura, R., et al., *Effect of a brief training program based on cognitive behavioral therapy in improving work performance: A randomized controlled trial.* Journal of occupational health, 2015. **57**(2): p. 169-178.

237. Kishita, N. and K. Laidlaw, *Cognitive behaviour therapy for generalized anxiety disorder: Is CBT equally efficacious in adults of working age and older adults?* Clinical psychology review, 2017. **52**: p. 124-136.

238. Danielsson, L., M. Elf, and G. Hensing, *Strategies to keep working among workers with common mental disorders–a grounded theory study.* Disability and rehabilitation, 2019. **41**(7): p. 786-795.

239. Danielsson, L., et al., *Work-directed rehabilitation or physical activity to support work ability and mental health in common mental disorders: a pilot randomized controlled trial.* Clinical Rehabilitation, 2020. **34**(2): p. 170-181.

240. Demou, E., et al., *Evaluating sickness absence duration by musculoskeletal and mental health issues: a retrospective cohort study of Scottish healthcare workers.* BMJ open, 2018. **8**(1): p. e018085.

241. Deppermann, S., et al., *Neurobiological and clinical effects of fNIRS-controlled rTMS in patients with panic disorder/agoraphobia during cognitive-behavioural therapy.* NeuroImage: Clinical, 2017. **16**: p. 668-677.

242. Doki, S., S. Sasahara, and I. Matsuzaki, *Psychological approach of occupational health service to sick leave due to mental problems: a systematic review and meta-analysis.* International archives of occupational and environmental health, 2015. **88**(6): p. 659-667.

243. Gragnano, A., et al., *Common psychosocial factors predicting return to work after common mental disorders, cardiovascular diseases, and cancers: a review of reviews supporting a cross-disease approach.* Journal of occupational rehabilitation, 2018. **28**(2): p. 215-231.

244. Grimholt, T.K., et al., *Flight anxiety reported from 1986 to 2015.* Aerospace medicine and human performance, 2019. **90**(4): p. 384-388.

245. MI, G.L., *Clinical Psychologist in Primary Care: The work carried out in Asturias.* Semergen, 2019. **46**(2): p. 101-106.

246. Halaj, A., et al., *Utilization of learned skills in cognitive behavioural therapy for panic disorder.* Behavioural and cognitive psychotherapy, 2019. **47**(6): p. 645-658.

247. Ontario, H.Q., *Psychotherapy for major depressive disorder and generalized anxiety disorder: a health technology assessment.* Ontario health technology assessment series, 2017. **17**(15): p. 1.

248. Heron-Delaney, M., J. Warren, and J.A. Kenardy, *Predictors of non-return to work 2 years post-injury in road traffic crash survivors: results from the UQ SuPPORT study.* Injury, 2017. **48**(6): p. 1120-1128.

249. Howlett, J.R. and M.P. Paulus, *Where perception meets belief updating: Computational evidence for slower updating of visual expectations in anxious individuals.* Journal of Affective Disorders, 2020. **266**: p. 633-638.

250. Horenstein, A. and R.G. Heimberg, *Anxiety disorders and healthcare utilization: A systematic review.* Clinical Psychology Review, 2020: p. 101894.

Copyright ©2021 Reed Group, Ltd.

251. Ikic, V., et al., *Reduction in Costs after Treating Comorbid Panic Disorder with Agoraphobia and Generalized Anxiety Disorder.* The Journal of Mental Health Policy and Economics, 2017. **20**(1): p. 11-20.

252. Jacoby, S.F., J. Shults, and T.S. Richmond, *The effect of early psychological symptom severity on long-term functional recovery: A secondary analysis of data from a cohort study of minor injury patients.* International journal of nursing studies, 2017. **65**: p. 54-61.

253. Joyce, S., et al., *Workplace interventions for common mental disorders: a systematic meta-review.* Psychological medicine, 2016. **46**(4): p. 683-697.

254. Kausto, J., et al., *Length of sickness absence and sustained return-to-work in mental disorders and musculoskeletal diseases: a cohort study of public sector employees.* Scandinavian Journal of Work, Environment & Health, 2017: p. 358-366.

255. Knapstad, M., T. Nordgreen, and O.R. Smith, *Prompt mental health care, the Norwegian version of IAPT: clinical outcomes and predictors of change in a multicenter cohort study.* BMC psychiatry, 2018. **18**(1): p. 260.

256. Knapstad, M., et al., *Prompt Mental Health Care (PMHC): work participation and functional status at 12 months post-treatment.* BMC health services research, 2020. **20**(1): p. 85.

257. Kunzler, A.M., et al., *Psychological interventions to foster resilience in healthcare students.* Cochrane Database of Systematic Reviews, 2020(7).

258. Lefkowitz, R.Y., et al., *Injury, illness, and mental health risks in United States domestic mariners.* Journal of Occupational and Environmental Medicine, 2020. **62**(10): p. 839-841.

259. Linden, M., et al., *Treatment Changes in General Practice Patients With Chronic Mental Disorders Following a Psychiatric–Psychosomatic Consultation.* Health services research and managerial epidemiology, 2018. **5**: p. 2333392818758523.

260. Maurer, F., et al., *Effectiveness of CBT on Unemployed Compared to Employed Individuals Suffering from Prevalent Mental Disorders-A Naturalistic Study.* Psychotherapie, Psychosomatik, Medizinische Psychologie, 2017. **67**(2): p. 66-75.

261. Mazza, C., et al., *Indicators to distinguish symptom accentuators from symptom producers in individuals with a diagnosed adjustment disorder: A pilot study on inconsistency subtypes using SIMS and MMPI-2-RF.* PloS one, 2019. **14**(12): p. e0227113.

262. McDevitt-Petrovic, O., M. Shevlin, and K. Kirby, *Modelling changes in anxiety and depression during low-intensity cognitive behavioural therapy: An application of growth mixture models.* British Journal of Clinical Psychology, 2020. **59**(2): p. 169-185.

263. McEvoy, P.M., et al., *Transportability of imagery-enhanced CBT for social anxiety disorder.* Behaviour research and therapy, 2018. **106**: p. 86-94.

264. Meunier, S., et al., *Feeling better at work! Mental health self-management strategies for workers with depressive and anxiety symptoms.* Journal of affective disorders, 2019. **254**: p. 7-14.

265. Vergallo, G.M., G. Bersani, and R. Rinaldi, *CoViD-19 and psychiatry: can mental illness justify further exceptions to the obligation to stay at home?* Rivista di psichiatria, 2020. **55**(4): p. 245-249.

266. Rubel, J.A., et al., *The working alliance in manualized CBT for generalized anxiety disorder: Does it lead to change and does the effect vary depending on manual implementation flexibility?* Journal of consulting and clinical psychology, 2019. **87**(11): p. 989.

267. Rudkjoebing, L.A., et al., *Work-Related exposure to violence or threats and risk of mental disorders and symptoms: a systematic review and meta-analysis.* Scand J Work Environ Health, 2020.

Copyright ©2021 Reed Group, Ltd.

268. Nigatu, Y., et al., *Interventions for enhancing return to work in individuals with a common mental illness: systematic review and meta-analysis of randomized controlled trials.* Psychological medicine, 2016. **46**(16): p. 3263-3274.

269. Poulsen, R., et al., *Integrated mental health care and vocational rehabilitation to improve return to work rates for people on sick leave because of exhaustion disorder, adjustment disorder, and distress (the Danish IBBIS trial): study protocol for a randomized controlled trial.* Trials, 2017. **18**(1): p. 579.

270. Roberge, P., et al., *A pragmatic randomized controlled trial of group transdiagnostic cognitive-behaviour therapy for anxiety disorders in primary care: study protocol.* BMC psychiatry, 2018. **18**(1): p. 320.

271. Williams, M.D., et al., *A quality improvement project aimed at adapting primary care to ensure the delivery of evidence-based psychotherapy for adult anxiety.* BMJ open quality, 2018. **7**(1).

272. Apolinário-Hagen, J., M. Drüge, and L. Fritsche, *Cognitive Behavioral Therapy, Mindfulness-Based Cognitive Therapy and Acceptance Commitment Therapy for Anxiety Disorders: Integrating Traditional with Digital Treatment Approaches*, in *Anxiety Disorders*. 2020, Springer. p. 291-329.

273. Boswell, J.F., et al., *Behavioral activation strategies in cognitive-behavioral therapy for anxiety disorders.* Psychotherapy, 2017. **54**(3): p. 231.

274. Constantino, M.J., et al., *Specific and common processes as mediators of the long-term effects of cognitive-behavioral therapy integrated with motivational interviewing for generalized anxiety disorder.* Psychotherapy Research, 2019. **29**(2): p. 213-225.

275. Egger, N., et al., *Long-term cost-effectiveness of cognitive behavioral therapy versus psychodynamic therapy in social anxiety disorder.* Depression and Anxiety, 2016. **33**(12): p. 1114-1122.

276. Tirpak, J.W., et al., *Changes in positive affect in cognitive-behavioral treatment of anxiety disorders.* General Hospital Psychiatry, 2019. **61**: p. 111-115.

277. Yoshinaga, N., et al., *Cognitive behavioral therapy for patients with social anxiety disorder who remain symptomatic following antidepressant treatment: a randomized, assessor-blinded, controlled trial.* Psychotherapy and psychosomatics, 2016. **85**(4): p. 208-217.

278. Bortolon, C., et al., *The roles of cognitive avoidance, rumination and negative affect in the association between abusive supervision in the workplace and non-clinical paranoia in a sample of workers working in France.* Psychiatry research, 2019. **271**: p. 581-589.

279. Brenninkmeijer, V., et al., *Predicting the effectiveness of work-focused CBT for common mental disorders: The influence of baseline self-efficacy, depression and anxiety.* Journal of occupational rehabilitation, 2019. **29**(1): p. 31-41.

280. Dalgaard, V.L., et al., *Return to work after work-related stress: a randomized controlled trial of a work-focused cognitive behavioral intervention.* Scandinavian Journal of Work, Environment & Health, 2017: p. 436-446.

281. Ebrahim, S., *Psychotherapy for depression in claimants receiving wage replacement benefits: review of the evidence.* Journal of insurance medicine (New York, NY), 2014. **44**(1): p. 53-57.

282. Gjengedal, R.G., et al., *Work-focused therapy for common mental disorders: A naturalistic study comparing an intervention group with a waitlist control group.* Work, 2020(Preprint): p. 1-11.

283. Himle, J.A., et al., *Study protocol: A multisite trial of Work-Related Cognitive behavioral therapy for unemployed persons with social anxiety.* Contemporary clinical trials communications, 2019. **16**: p. 100464.

284. Ito, D., et al., *A Preliminary study of work-focused cognitive behavioural group therapy for Japanese workers.* Behavioural and cognitive psychotherapy, 2019. **47**(2): p. 251-256.

Copyright ©2021 Reed Group, Ltd.

285. Johnsen, T.L., et al., *Work and mental complaints: are response outcome expectancies more important than work conditions and number of subjective health complaints?* Journal of Occupational Rehabilitation, 2017. **27**(2): p. 218-227.

286. Wormgoor, M., et al., *Effectiveness of briefer coping-focused psychotherapy for common mental complaints on work-participation and mental health: a pragmatic randomized trial with 2-year follow-up.* Journal of occupational rehabilitation, 2020. **30**(1): p. 22-39.

287. Dewa, C.S., et al., *The effectiveness of return-to-work interventions that incorporate work-focused problem-solving skills for workers with sickness absences related to mental disorders: a systematic literature review.* BMJ open, 2015. **5**(6): p. e007122.

288. Salomonsson, S., et al., *Effects of cognitive behavioural therapy and return-to-work intervention for patients on sick leave due to stress-related disorders: Results from a randomized trial.* Scandinavian Journal of Psychology, 2020. **61**(2): p. 281-289.

289. Salzwedel, A., et al., *Patients' expectations of returning to work, co-morbid disorders and work capacity at discharge from cardiac rehabilitation.* Vascular Health and Risk Management, 2019. **15**: p. 301.

290. Schofield, C.A., G.T. Ponzini, and S.J. Becker, *Evaluating approaches to marketing cognitive behavioral therapy: does evidence matter to consumers?* Cognitive Behaviour Therapy, 2020: p. 1-13.

291. Shepardson, R.L., M.R. Minnick, and J.S. Funderburk, *Anxiety interventions delivered in primary care behavioral health routine clinical practice.* Families, Systems, & Health, 2020. **38**(2): p. 193.

292. Sewart, A.R., et al., *Examining positive and negative affect as outcomes and moderators of cognitive-behavioral therapy and acceptance and commitment therapy for social anxiety disorder.* Behavior Therapy, 2019. **50**(6): p. 1112-1124.

293. Smith, B.M., G.S. Smith, and S. Dymond, *Relapse of anxiety-related fear and avoidance: Conceptual analysis of treatment with acceptance and commitment therapy.* Journal of the experimental analysis of behavior, 2020. **113**(1): p. 87-104.

294. Spagnolo, J., et al., *Mental health knowledge, attitudes, and self-efficacy among primary care physicians working in the Greater Tunis area of Tunisia.* International journal of mental health systems, 2018. **12**(1): p. 63.

295. Song, L., et al., *Mental health and work attitudes among people resuming work during the COVID-19 pandemic: A cross-sectional study in china.* International journal of environmental research and public health, 2020. **17**(14): p. 5059.

296. Springer, K.S., H.C. Levy, and D.F. Tolin, *Remission in CBT for adult anxiety disorders: A meta-analysis.* Clinical psychology review, 2018. **61**: p. 1-8.

297. Stefan, S., et al., *Cognitive-behavioral therapy (CBT) for generalized anxiety disorder: Contrasting various CBT approaches in a randomized clinical trial.* Journal of clinical psychology, 2019. **75**(7): p. 1188-1202.

298. Tan, W., et al., *Is returning to work during the COVID-19 pandemic stressful? A study on immediate mental health status and psychoneuroimmunity prevention measures of Chinese workforce.* Brain, behavior, and immunity, 2020.

299. Markowitz, J.C. and M.M. Weissman, *Interpersonal psychotherapy: principles and applications.* World psychiatry : official journal of the World Psychiatric Association (WPA), 2004. **3**(3): p. 136-139.

300. Lagerveld, S.E., et al., *Work-focused treatment of common mental disorders and return to work: a comparative outcome study.* Journal of occupational health psychology, 2012. **17**(2): p. 220.

301. Ojala, B., et al., *A cognitive behavioural intervention programme to improve psychological well-being.* International journal of environmental research and public health, 2019. **16**(1): p. 80.

Copyright ©2021 Reed Group, Ltd.

302. Reme, S.E., et al., *Work-focused cognitive–behavioural therapy and individual job support to increase work participation in common mental disorders: a randomised controlled multicentre trial.* Occupational and environmental medicine, 2015. **72**(10): p. 745-752.

303. Sasaki, N., et al., *Effects of brief communication skills training for workers based on the principles of cognitive behavioral therapy: a randomized controlled trial.* Journal of Occupational and Environmental Medicine, 2017. **59**(1): p. 61.

304. Wagner, S., et al., *Mental health interventions in the workplace and work outcomes: a best-evidence synthesis of systematic reviews.* The international journal of occupational and environmental medicine, 2016. **7**(1): p. 1.

305. Winter, L., et al., *Return to Work: A Workplace Focused Module to be Integrated in Cognitive Behavioral Therapy.* Psychotherapie, Psychosomatik, medizinische Psychologie, 2015. **65**(8): p. 321-326.

306. Becker-Haimes, E.M., et al., *Predictors of clinician use of exposure therapy in community mental health settings.* Journal of anxiety disorders, 2017. **49**: p. 88-94.

307. Becker-Haimes, E.M., et al., *Identifying the organizational innovation-specific capacity needed for exposure therapy.* Depression and Anxiety, 2020.

308. Bjertnaes, O. and H.H. Iversen, *Inpatients' assessment of outcome at psychiatric institutions: an analysis of predictors following a national cross-sectional survey in Norway.* BMJ open, 2018. **8**(12).

309. Stanley, I.H., et al., *Anxiety sensitivity and suicidal ideation/suicide risk: A meta-analysis.* J Consult Clin Psychol, 2018. **86**(11): p. 946-960.

310. Bolton, J.M., D. Gunnell, and G. Turecki, *Suicide risk assessment and intervention in people with mental illness.* Bmj, 2015. **351**: p. h4978.

311. Kanwar, A., et al., *The association between anxiety disorders and suicidal behaviors: A systematic review and meta-analysis.* Depression and anxiety, 2013. **30**(10): p. 917-929.

312. Marco, J.H., S. Alonso, and J. Andani, *Early intervention with cognitive behavioral therapy reduces sick leave duration in people with adjustment, anxiety and depressive disorders.* Journal of Mental Health, 2018.

313. Naidu, V., et al., *Delivery of cognitive behavioural therapy to workers: a systematic review.* Occupational Medicine, 2016. **66**(2): p. 112-117.

314. Alonso, S., J.H. Marco, and J. Andani, *Reducing the time until psychotherapy initiation reduces sick leave duration in participants diagnosed with anxiety and mood disorders.* Clinical psychology & psychotherapy, 2018. **25**(1): p. 138-143.

315. Andersén, Å., et al., *Predictors of self-efficacy in women on long-term sick leave.* International Journal of Rehabilitation Research, 2015. **38**(4): p. 320-326.

316. Arends, I., et al., *One-year trajectories of mental health and work outcomes post return to work in patients with common mental disorders.* Journal of affective disorders, 2019. **257**: p. 263-270.

317. Brämberg, E.B., et al., *Facilitators, barriers and ethical values related to the coordination of return-to-work among employees on sick leave due to common mental disorders: a protocol for a qualitative study (the CORE-project).* BMJ open, 2019. **9**(9): p. e032463.

318. Boini, S., et al., *Is the effect of work-related psychosocial exposure on depressive and anxiety disorders short-term, lagged or cumulative?* International Archives of Occupational and Environmental Health, 2020. **93**(1): p. 87-104.

319. Fan, J.K., C. Mustard, and P.M. Smith, *Psychosocial work conditions and mental health: examining differences across mental illness and well-being outcomes.* Annals of Work Exposures and Health, 2019. **63**(5): p. 546-559.

Copyright ©2021 Reed Group, Ltd.

320. Lau, B., et al., *What are they returning to? Psychosocial work environment as a predictor of returning to work among employees in treatment for common mental disorders: A prospective observational pre–post study.* PloS one, 2019. **14**(4): p. e0215354.

321. Løvvik, C., et al., *Association between illness perceptions and return-to-work expectations in workers with common mental health symptoms.* Journal of occupational rehabilitation, 2014. **24**(1): p. 160-170.

322. Løvvik, C., et al., *Expectations and illness perceptions as predictors of benefit recipiency among workers with common mental disorders: secondary analysis from a randomised controlled trial.* BMJ open, 2014. **4**(3).

323. Hees, H.L., et al., *Towards a new definition of return-to-work outcomes in common mental disorders from a multi-stakeholder perspective.* PLoS One, 2012. **7**(6): p. e39947.

324. Neves, R.d.F., M.d.O. Nunes, and L. Magalhães, *Interactions among stakehoklders involved in return to work after sick leave due to mental disorders: a meta-ethnography.* Cadernos de Saúde Pública, 2015. **31**: p. 2275-2290.

325. Pedersen, P., et al., *Psychoeducation to facilitate return to work in individuals on sick leave and at risk of having a mental disorder: protocol of a randomised controlled trial.* BMC Public Health, 2014. **14**(1): p. 1288.

326. Sheehan, L.R., et al., *Factors associated with employer support for injured workers during a workers' compensation claim.* Journal of occupational rehabilitation, 2019. **29**(4): p. 718-727.

327. Parker, Z.J. and G. Waller, *Development and validation of the Negative Attitudes towards CBT Scale.* Behavioural and Cognitive Psyhotherapy, 2017.

328. Victor, M., B. Lau, and T. Ruud, *Predictors of return to work among patients in treatment for common mental disorders: a pre-post study.* BMC public health, 2018. **18**(1): p. 27.

329. Victor, M., B. Lau, and T. Ruud, *Predictors of return to work 6 months after the end of treatment in patients with common mental disorders: A cohort study.* Journal of occupational rehabilitation, 2018. **28**(3): p. 548-558.

330. Durand, M.-J., et al., *A review of best work-absence management and return-to-work practices for workers with musculoskeletal or common mental disorders.* Work, 2014. **48**(4): p. 579-589.

331. van Beurden, K.M., et al., *Effect of an intervention to enhance guideline adherence of occupational physicians on return-to-work self-efficacy in workers sick-listed with common mental disorders.* BMC Public Health, 2015. **15**(1): p. 796.

332. Buys, N.J., J. Selander, and J. Sun, *Employee experience of workplace supervisor contact and support during long-term sickness absence.* Disability and Rehabilitation, 2019. **41**(7): p. 808-814.

333. Cornelius, L., et al., *High prevalence of early onset mental disorders among long-term disability claimants.* Disability and rehabilitation, 2016. **38**(6): p. 520-527.

334. Edlund, M.J., et al., *Which mental disorders are associated with the greatest impairment in functioning?* Social psychiatry and psychiatric epidemiology, 2018. **53**(11): p. 1265-1276.

335. Eklund, M., *Minor long-term effects 3-4 years after the ReDO™ intervention for women with stress-related disorders: A focus on sick leave rate, everyday occupations and well-being.* Work, 2017. **58**(4): p. 527-536.

336. Juurlink, T.T., et al., *The role of borderline personality disorder symptoms on absenteeism & work performance in the Netherlands Study of Depression and Anxiety (NESDA).* BMC psychiatry, 2020. **20**(1): p. 1-10.

337. Lagerveld, S.E., et al., *Predictive value of work-related self-efficacy change on RTW for employees with common mental disorders.* Occupational and environmental medicine, 2017. **74**(5): p. 381-383.

Copyright ©2021 Reed Group, Ltd.

338. Lam, R.W., et al., *Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 clinical guidelines for the management of adults with major depressive disorder: section 1. Disease burden and principles of care.* The Canadian Journal of Psychiatry, 2016. **61**(9): p. 510-523.

339. Lammerts, L., et al., *Return to work of workers without a permanent employment contract, sick-listed due to a common mental disorder: design of a randomised controlled trial.* BMC Public Health, 2014. **14**(1): p. 594.

340. Lammerts, L., et al., *Longitudinal associations between biopsychosocial factors and sustainable return to work of sick-listed workers with a depressive or anxiety disorder.* Journal of occupational rehabilitation, 2016. **26**(1): p. 70-79.

341. Lemogne, C., et al., *Prognosis of anxiety disorders.* La Revue du Praticien, 2019. **69**(9): p. 979-980.

342. Muschalla, B., *Negative work perception not changed in a short work-anxiety-coping group therapy intervention.* International journal of occupational and environmental health, 2016. **22**(4): p. 321-324.

343. Muschalla, B., M. Linden, and M. Jöbges, *Work-anxiety and sickness absence after a short inpatient cognitive behavioral group intervention in comparison to a recreational group meeting.* Journal of occupational and environmental medicine, 2016. **58**(4): p. 398-406.

344. Nigatu, Y.T., et al., *Prognostic factors for return to work of employees with common mental disorders: a meta-analysis of cohort studies.* Social psychiatry and psychiatric epidemiology, 2017. **52**(10): p. 1205-1215.

345. Norder, G., et al., *External validation and update of a prediction rule for the duration of sickness absence due to common mental disorders.* Journal of occupational rehabilitation, 2017. **27**(2): p. 202-209.

346. Bomyea, J., et al., *Change in neural response during emotion regulation is associated with symptom reduction in cognitive behavioral therapy for anxiety disorders.* Journal of Affective Disorders, 2020.

347. Ellard, K.K., et al., *Neural correlates of emotion acceptance vs worry or suppression in generalized anxiety disorder.* Social cognitive and affective neuroscience, 2017. **12**(6): p. 1009-1021.

348. Association, A.P. *Diagnostic and statistical manual of mental disorders*. 2013; 5th ed.:[

349. Organization, W.H. *The ICD-10 Classification of Mental and Behavioural Disorders*. 2016; Available from: https://www.who.int/classifications/icd/en/bluebook.pdf.

350. Beck, A.T., et al., *An inventory for measuring clinical anxiety: psychometric properties.* Journal of consulting and clinical psychology, 1988. **56**(6): p. 893.

351. Hewitt, P.L. and G.R. Norton, *The Beck Anxiety Inventory: A psychometric analysis.* Psychological Assessment, 1993. **5**(4): p. 408.

352. Creamer, M., J. Foran, and R. Bell, *The Beck Anxiety Inventory in a non-clinical sample.* Behaviour research and Therapy, 1995. **33**(4): p. 477-485.

353. Gillis, M.M., D.A. Haaga, and G.T. Ford, *Normative values for the beck anxiety inventory, fear questionnaire, Penn state worry questionnaire, and social phobia and anxiety inventory.* Psychological Assessment, 1995. **7**(4): p. 450.

354. Beck, A.T., et al., *Use of the Beck Anxiety and Depression Inventories for primary care with medical outpatients.* Assessment, 1997. **4**(3): p. 211-219.

355. Hoyer, J., et al., *Screening for anxiety in an epidemiological sample: predictive accuracy of questionnaires.* Journal of Anxiety Disorders, 2002. **16**(2): p. 113-134.

356. Leyfer, O.T., J.L. Ruberg, and J. Woodruff-Borden, *Examination of the utility of the Beck Anxiety Inventory and its factors as a screener for anxiety disorders.* Journal of Anxiety Disorders, 2006. **20**(4): p. 444-458.

Copyright ©2021 Reed Group, Ltd.

357. Eack, S.M., J.B. Singer, and C.G. Greeno, *Screening for anxiety and depression in community mental health: the beck anxiety and depression inventories.* Community mental health journal, 2008. **44**(6): p. 465-474.

358. Muntingh, A.D., et al., *Is the beck anxiety inventory a good tool to assess the severity of anxiety? A primary care study in The Netherlands study of depression and anxiety (NESDA).* BMC family practice, 2011. **12**(1): p. 66.

359. Zimmerman, M., et al., *A clinically useful anxiety outcome scale.* The Journal of clinical psychiatry, 2010. **71**(5): p. 534-542.

360. Dalrymple, K., et al., *A clinically useful social anxiety disorder outcome scale.* Comprehensive psychiatry, 2013. **54**(7): p. 758-765.

361. Spitzer, R.L., et al., *A brief measure for assessing generalized anxiety disorder: the GAD-7.* Archives of internal medicine, 2006. **166**(10): p. 1092-1097.

362. Swinson, R., *The GAD-7 scale was accurate for diagnosing generalised anxiety disorder.* Evidence-based medicine, 2006. **11**(6): p. 184.

363. Kroenke, K., et al., *The patient health questionnaire somatic, anxiety, and depressive symptom scales: a systematic review.* General hospital psychiatry, 2010. **32**(4): p. 345-359.

364. Homans, W., *The validity of the PHQ-9 and the GAD-7 for screening depressive and anxiety disorders in sick-listed workers*. 2012.

365. Kertz, S., J. Bigda-Peyton, and T. Bjorgvinsson, *Validity of the Generalized Anxiety Disorder-7 Scale in an acute psychiatric sample.* Clinical psychology & psychotherapy, 2013. **20**(5): p. 456-464.

366. Ryan, T.A., et al., *Factorial invariance of the patient health questionnaire and generalized anxiety disorder questionnaire.* British Journal of Clinical Psychology, 2013. **52**(4): p. 438-449.

367. Beard, C. and T. Björgvinsson, *Beyond generalized anxiety disorder: psychometric properties of the GAD-7 in a heterogeneous psychiatric sample.* Journal of Anxiety Disorders, 2014. **28**(6): p. 547-552.

368. Henderson, L.C., M.M. Antony, and N. Koerner, *Psychometric properties of the Generalized Anxiety Disorder Inventory in a Canadian sample.* Journal of psychopharmacology, 2014. **28**(5): p. 440-448.

369. Herr, N.R., et al., *Does this patient have generalized anxiety or panic disorder?: The Rational Clinical Examination systematic review.* JAMA, 2014. **312**(1): p. 78-84.

370. Plummer, F., et al., *Screening for anxiety disorders with the GAD-7 and GAD-2: a systematic review and diagnostic metaanalysis.* General hospital psychiatry, 2016. **39**: p. 24-31.

371. Silva, M.T., et al., *Generalized anxiety disorder and associated factors in adults in the Amazon, Brazil: A population-based study.* Journal of affective disorders, 2018. **236**: p. 180-186.

372. Bruss, G.S., et al., *Hamilton Anxiety Rating Scale Interview guide: joint interview and test-retest methods for interrater reliability.* Psychiatry research, 1994. **53**(2): p. 191-202.

373. Shear, M.K., et al., *Reliability and validity of a structured interview guide for the Hamilton Anxiety Rating Scale (SIGH-A).* Depression and anxiety, 2001. **13**(4): p. 166-178.

374. Tural, Ü., et al., *Assessing the severity of panic disorder and agoraphobia:: Validity, reliability and objectivity of the Turkish translation of the Panic and Agoraphobia Scale (P&A).* Journal of anxiety disorders, 2002. **16**(3): p. 331-340.

375. Osone, A. and S. Takahashi, *Putative temperament of patients with generalized anxiety disorder: Two-years' interval test–retest reliability of a Japanese version of the Generalized Anxious Temperament.* Psychiatry and clinical neurosciences, 2006. **60**(1): p. 96-102.

Copyright ©2021 Reed Group, Ltd.

376. Ruiz, M.A., et al., *Validity of the GAD-7 scale as an outcome measure of disability in patients with generalized anxiety disorders in primary care.* Journal of affective disorders, 2011. **128**(3): p. 277-286.

377. Donzuso, G., et al., *The neuroanatomical correlates of anxiety in a healthy population: differences between the State-Trait Anxiety Inventory and the Hamilton Anxiety Rating Scale.* Brain and behavior, 2014. **4**(4): p. 504-514.

378. Olariu, E., et al., *Validation of clinical symptom IRT scores for diagnosis and severity assessment of common mental disorders.* Quality of Life Research, 2015. **24**(4): p. 979-992.

379. Porter, E., et al., *Psychometric properties of the reconstructed Hamilton depression and anxiety scales.* The Journal of nervous and mental disease, 2017. **205**(8): p. 656.

380. Zimmerman, M., et al., *Reliability and validity of a self-report scale for daily assessments of the severity of anxiety symptoms.* Comprehensive psychiatry, 2019. **90**: p. 37-42.

381. Schalet, B.D., et al., *Clinical validity of PROMIS depression, anxiety, and anger across diverse clinical samples.* Journal of clinical epidemiology, 2016. **73**: p. 119-127.

382. Pilkonis, P.A., et al., *Patient-Reported Outcomes Measurement Information System.* Assessment, 2011.

383. Pilkonis, P.A., et al., *Item banks for measuring emotional distress from the Patient-Reported Outcomes Measurement Information System (PROMIS®): depression, anxiety, and anger.* Assessment, 2011. **18**(3): p. 263-283.

384. Purvis, T.E., et al., *Comparison of PROMIS Anxiety and Depression, PHQ-8, and GAD-7 to screen for anxiety and depression among patients presenting for spine surgery.* Journal of Neurosurgery: Spine, 2019. **30**(4): p. 524-531.

385. Choi, S.W., et al., *Establishing a common metric for depressive symptoms: linking the BDI-II, CES-D, and PHQ-9 to PROMIS depression.* Psychol Assess, 2014. **26**(2): p. 513-27.

386. Sharma, M., et al., *Concurrent validity and comparative responsiveness of PROMIS-SF versus legacy measures in the cervical and lumbar spine population: longitudinal analysis from baseline to postsurgery.* World neurosurgery, 2018. **115**: p. e664-e675.

387. Beleckas, C.M., et al., *Anxiety in the orthopedic patient: using PROMIS to assess mental health.* Quality of Life Research, 2018. **27**(9): p. 2275-2282.

388. Sunderland, M., et al., *Validity of the PROMIS depression and anxiety common metrics in an online sample of Australian adults.* Quality of Life Research, 2018. **27**(9): p. 2453-2458.

389. Boulton, A.J., et al., *Linking the GAD-7 and PHQ-9 to the TBI-QOL Anxiety and Depression Item Banks.* The Journal of head trauma rehabilitation, 2019. **34**(5): p. 353-363.

390. Kroenke, K., F. Baye, and S.G. Lourens, *Comparative responsiveness and minimally important difference of common anxiety measures.* Medical care, 2019. **57**(11): p. 890-897.

391. Hays, R.D., et al., *PROMIS®-29 v2. 0 profile physical and mental health summary scores.* Quality of life Research, 2018. **27**(7): p. 1885-1891.

392. Tarescavage, A.M., E.H. Forner, and Y. Ben-Porath, *Construct Validity of DSM-5 Level 2 Assessments (PROMIS Depression, Anxiety, and Anger): Evidence From the MMPI-2-RF.* Assessment, 2020: p. 1073191120911092.

393. Abend, R., et al., *Reliability, validity and sensitivity of a computerized visual analog scale measuring state anxiety.* Journal of Behavior Therapy and Experimental Psychiatry, 2014. **45**(4): p. 447-453.

394. Andrade, L., et al., *Psychometric properties of the Portuguese version of the State-Trait Anxiety Inventory applied to college students: factor analysis and relation to the Beck Depression Inventory.* Brazilian Journal of Medical and Biological Research, 2001. **34**(3): p. 367-374.

Copyright ©2021 Reed Group, Ltd.

395. Barnes, L.L., D. Harp, and W.S. Jung, *Reliability generalization of scores on the Spielberger state-trait anxiety inventory.* Educational and psychological measurement, 2002. **62**(4): p. 603-618.

396. Bieling, P.J., M.M. Antony, and R.P. Swinson, *The State--Trait Anxiety Inventory, Trait version: structure and content re-examined.* Behaviour research and therapy, 1998. **36**(7-8): p. 777-788.

397. Bunevicius, A., et al., *Screening for anxiety disorders in patients with coronary artery disease.* Health and quality of life outcomes, 2013. **11**(1): p. 37.

398. Grös, D.F., et al., *Psychometric properties of the State-Trait Inventory for Cognitive and Somatic Anxiety (STICSA): comparison to the State-Trait Anxiety Inventory (STAI).* Psychological assessment, 2007. **19**(4): p. 369.

399. Kabacoff, R.I., et al., *Psychometric properties and diagnostic utility of the Beck Anxiety Inventory and the State-Trait Anxiety Inventory with older adult psychiatric outpatients.* Journal of anxiety disorders, 1997. **11**(1): p. 33-47.

400. Kvaal, K., et al., *The Spielberger state-trait anxiety inventory (STAI): the state scale in detecting mental disorders in geriatric patients.* International Journal of Geriatric Psychiatry: A journal of the psychiatry of late life and allied sciences, 2005. **20**(7): p. 629-634.

401. Muschalla, B., M. Linden, and D. Olbrich, *The relationship between job-anxiety and trait-anxiety—A differential diagnostic investigation with the Job-Anxiety-Scale and the State-Trait-Anxiety-Inventory.* Journal of anxiety disorders, 2010. **24**(3): p. 366-371.

402. Van Dam, N.T., et al., *Establishing a trait anxiety threshold that signals likelihood of anxiety disorders.* Anxiety, Stress & Coping, 2013. **26**(1): p. 70-86.

403. van der Bij, A.K., et al., *Validation of the dutch short form of the state scale of the Spielberger State-Trait Anxiety Inventory: considerations for usage in screening outcomes.* Public Health Genomics, 2003. **6**(2): p. 84-87.

404. Adilay, U., et al., *The Correlation of SCL-90-R Anxiety, Depression, Somatization Subscale Scores with Chronic Low Back Pain.* Turk Neurosurg, 2018. **28**(3): p. 434-438.

405. Bech, P., et al., *The Hamilton scales and the Hopkins Symptom Checklist (SCL-90). A cross-national validity study in patients with panic disorders.* Br J Psychiatry, 1992. **160**: p. 206-11.

406. Bech, P., et al., *Psychometric validation of the Hopkins Symptom Checklist (SCL-90) subscales for depression, anxiety, and interpersonal sensitivity.* J Affect Disord, 2014. **160**: p. 98-103.

407. Bech, P. and N. Timmerby, *An overview of which health domains to consider and when to apply them in measurement-based care for depression and anxiety disorders.* Nord J Psychiatry, 2018. **72**(5): p. 367-373.

408. Berle, D., et al., *Do symptom interpretations mediate the relationship between panic attack symptoms and agoraphobic avoidance?* Behav Cogn Psychother, 2010. **38**(3): p. 275-89.

409. Goldberg, D.P., et al., *A comparison of two psychiatric screening tests.* The British Journal Of Psychiatry: The Journal Of Mental Science, 1976. **129**: p. 61-67.

410. Kirchmann, H., et al., *SCL-90-R symptom profile clusters among inpatients undergoing psychodynamic group psychotherapy: Cluster stability, associations with clinical characteristics and treatment outcome.* Psychopathology, 2011. **44**(2): p. 71-82.

411. Koeter, M.W., *Validity of the GHQ and SCL anxiety and depression scales: a comparative study.* J Affect Disord, 1992. **24**(4): p. 271-9.

412. Morgan, C.D., M.W. Wiederman, and R.D. Magnus, *Discriminant validity of the SCL-90 dimensions of anxiety and depression.* Assessment, 1998. **5**(2): p. 197-201.

Copyright ©2021 Reed Group, Ltd.

413. Schmitz, N., et al., *Diagnosing mental disorders in primary care: the General Health Questionnaire (GHQ) and the Symptom Check List (SCL-90-R) as screening instruments.* Social psychiatry and psychiatric epidemiology, 1999. **34**(7): p. 360-366.

414. Derogatis, L.R. and N. Melisaratos, *The brief symptom inventory: an introductory report.* Psychological medicine, 1983. **13**(3): p. 595-605.

415. Holden, R.R., et al., *Comparisons among the holden psychological screening inventory (HPSI), the brief symptom inventory (BSI), and the balanced inventory of desirable responding (BIDR).* Assessment, 2000. **7**(2): p. 163-175.

416. Lang, A.J., et al., *Abbreviated brief symptom inventory for use as an anxiety and depression screening instrument in primary care.* Depression and Anxiety, 2009. **26**(6): p. 537-543.

417. Schat, A., et al., *Concordance between self-reported and observer-rated anxiety severity in outpatients with anxiety disorders: The Leiden routine outcome monitoring study.* Psychology and Psychotherapy: Theory, Research and Practice, 2017. **90**(4): p. 705-719.

418. Staples, L.G., et al., *Psychometric properties and clinical utility of brief measures of depression, anxiety, and general distress: The PHQ-2, GAD-2, and K-6.* General hospital psychiatry, 2019. **56**: p. 13-18.

419. Hahn, D., K. Reuter, and M. Härter, *Screening for affective and anxiety disorders in medical patients-comparison of HADS, GHQ-12 and Brief-PHQ.* GMS Psycho-Social Medicine, 2006. **3**.

420. Kerper, L., et al., *Screening for depression, anxiety and general psychological distress in preoperative surgical patients: A psychometric analysis of the Patient Health Questionnaire 4 (PHQ-4).* Clin Health Promot, 2014. **4**(1): p. 5-14.

421. Khubchandani, J., et al., *The psychometric properties of PHQ-4 depression and anxiety screening scale among college students.* Archives of psychiatric nursing, 2016. **30**(4): p. 457-462.

422. Löwe, B., et al., *A 4-item measure of depression and anxiety: validation and standardization of the Patient Health Questionnaire-4 (PHQ-4) in the general population.* Journal of affective disorders, 2010. **122**(1-2): p. 86-95.

423. Cano-Vindel, A., et al., *A computerized version of the Patient Health Questionnaire-4 as an ultra-brief screening tool to detect emotional disorders in primary care.* Journal of affective disorders, 2018. **234**: p. 247-255.

424. Kroenke, K., et al., *Patient Health Questionnaire Anxiety and Depression Scale: Initial Validation in Three Clinical Trials.* Psychosomatic medicine, 2016. **78**(6): p. 716-727.

425. Wittkampf, K.A., et al., *The psychometric properties of the panic disorder module of the Patient Health Questionnaire (PHQ-PD) in high-risk groups in primary care.* Journal of affective disorders, 2011. **130**(1-2): p. 260-267.

426. Löwe, B., et al., *Detecting panic disorder in medical and psychosomatic outpatients: comparative validation of the Hospital Anxiety and Depression Scale, the Patient Health Questionnaire, a screening question, and physicians' diagnosis.* Journal of psychosomatic research, 2003. **55**(6): p. 515-519.

427. Cano, A., et al., *Mental health screening in primary care: a comparison of 3 brief measures of psychological distress.* Primary care companion to the Journal of clinical psychiatry, 2001. **3**(5): p. 206.

428. Kroenke, K., et al., *PROMIS 4-item measures and numeric rating scales efficiently assess SPADE symptoms compared with legacy measures.* Journal of Clinical Epidemiology, 2019. **115**: p. 116-124.

429. Bruns, D. and J.M. Disorbio, *The psychological evaluation of patients with chronic pain: a review of BHI 2 clinical and forensic interpretive considerations.* Psychological Injury and Law, 2014. **7**(4): p. 335-361.

430. Bruns, D. and J. Disorbio, *Battery for health improvement 2*. 2003, Minneapolis, MN, USA: Pearson.

Copyright ©2021 Reed Group, Ltd.

431. Hill, B.D., et al., *A psychometric evaluation of the STAI-Y, BDI-II, and PAI using single and multifactorial models in young adults seeking psychoeducational evaluation.* Journal of Psychoeducational Assessment, 2013. **31**(3): p. 300-312.

432. Slavin-Mulford, J., et al., *External validity of the Personality Assessment Inventory (PAI) in a clinical sample.* Journal of Personality Assessment, 2012. **94**(6): p. 593-600.

433. Rogers, R., et al., *Detection of feigned mental disorders on the Personality Assessment Inventory: A discriminant analysis.* Journal of personality assessment, 1996. **67**(3): p. 629-640.

434. Osma, J., et al., *Personality disorders among patients with panic disorder and individuals with high anxiety sensitivity.* Psicothema, 2014. **26**(2): p. 159-165.

435. Blais, M.A., et al., *Exploring the psychometric properties and construct validity of the MCMI-III anxiety and avoidant personality scales.* Journal of Personality Assessment, 2003. **81**(3): p. 237-241.

436. McDevitt-Murphy, M.E., et al., *The utility of the PAI and the MMPI-2 for discriminating PTSD, depression, and social phobia in trauma-exposed college students.* Assessment, 2007. **14**(2): p. 181-95.

437. Davis, S.E. and L.W. Hays, *An examination of the clinical validity of the MCMI-III Depressive Personality scale.* J Clin Psychol, 1997. **53**(1): p. 15-23.

438. Saulsman, L.M., *Depression, anxiety, and the MCMI-III: construct validity and diagnostic efficiency.* J Pers Assess, 2011. **93**(1): p. 76-83.

439. Arbisi, P.A. and Y.S. Ben-Porath, *An MMPI-2 infrequent response scale for use with psychopathological populations: The Infrequency-Psychopathology Scale, F(p).* Psychological Assessment, 1995. **7**(4): p. 424-431.

440. Arbisi, P.A., M. Sellbom, and Y.S. Ben-Porath, *Empirical correlates of the MMPI-2 Restructured Clinical (RC) Scales in psychiatric inpatients.* J Pers Assess, 2008. **90**(2): p. 122-8.

441. Archer, R.P., R. Griffin, and R. Aiduk, *MMPI-2 clinical correlates for ten common codes.* J Pers Assess, 1995. **65**(3): p. 391-407.

442. Bagby, R. and M. Marshall, *Assessing response bias with the MCMI modifying indices.* New Directions in Interpreting the Millon Clinical Multiaxial Inventory-III, 2005: p. 227-247.

443. Barthlow, D.L., et al., *The appropriateness of the MMPI-2 K correction.* Assessment, 2002. **9**(3): p. 219-29.

444. Bence, V.M., et al., *Differential sensitivity of the MMPI-2 depression scales and subscales.* J Clin Psychol, 1995. **51**(3): p. 375-7.

445. Ben-Porath, Y.S., J.N. Butcher, and J.R. Graham, *Contribution of the MMPI-2 content scales to the differential diagnosis of schizophrenia and major depression.* Psychological Assessment: A Journal of Consulting and Clinical Psychology, 1991. **3**(4): p. 634-640.

446. Ben-Porath, Y.S., *Interpreting the MMPI-2-RF*. Interpreting the MMPI-2-RF. 2012, Minneapolis, MN, US: University of Minnesota Press. xvi, 534-xvi, 534.

447. Binford, A. and L. Liljequist, *Behavioral correlates of selected MMPI-2 clinical, content, and restructured clinical scales.* J Pers Assess, 2008. **90**(6): p. 608-14.

448. Blasco Saiz, J.L. and L. Pallardó Durá, *Detección de exageración de síntomas mediante el SIMS y el MMPI-2-RF en pacientes diagnosticados de trastorno mixto ansioso-depresivo y adaptativo en el contexto medicolegal: un estudio preliminar.* Clínica y Salud, 2013. **24**(3): p. 177-183.

449. Boone, D., *Differential validity of the MMPI-2 Subtle and Obvious scales with psychiatric inpatients: scale 2.* J Clin Psychol, 1995. **51**(4): p. 526-31.

Copyright ©2021 Reed Group, Ltd.

450. Egger, J.I., P.A. Delsing, and H.R. De Mey, *Differential diagnosis using the MMPI-2: Goldberg's index revisited.* Eur Psychiatry, 2003. **18**(8): p. 409-11.

451. Hersch, P.D. and R.W. Alexander, *MMPI profile patterns of emotional disability claimants.* J Clin Psychol, 1990. **46**(6): p. 795-9.

452. McGrath, R.E., D. Powis, and D.L. Pogge, *Code type-specific tables for interpretation of MMPI-2 Harris and Lingoes subscales: consideration of gender and code type definition.* J Clin Psychol, 1998. **54**(5): p. 655-64.

453. Tsushima, W.T., O. Geling, and J. Fabrigas, *Comparison of MMPI-2 validity scale scores of personal injury litigants and disability claimants.* Clin Neuropsychol, 2011. **25**(8): p. 1403-14.

454. Zalewski, C., et al., *Discriminant validity of the MMPI Depression Subtle (DS) and Depression Obvious (DO) scales.* Assessment, 1997. **4**(4): p. 311-319.

455. Aikman, G.G. and G.T. Souheaver, *Use of the Personality Assessment Inventory (PAI) in neuropsychological testing of psychiatric outpatients.* Appl Neuropsychol, 2008. **15**(3): p. 176-83.

456. Boone, D., *Internal consistency reliability of the Personality Assessment Inventory with psychiatric inpatients.* Journal of Clinical Psychology, 1998. **54**(6): p. 839-843.

457. Frazier, T.W., R.I. Naugle, and K.A. Haggerty, *Psychometric adequacy and comparability of the short and full forms of the Personality Assessment Inventory.* Psychol Assess, 2006. **18**(3): p. 324-33.

458. Gaines, M.V., C.L. Giles, and R.D. Morgan, *The detection of feigning using multiple PAI scale elevations: a new index.* Assessment, 2013. **20**(4): p. 437-47.

459. Haggerty, K.A., et al., *Relationships among victoria symptom validity test indices and personality assessment inventory validity scales in a large clinical sample.* Clin Neuropsychol, 2007. **21**(6): p. 917-28.

460. Handel, R.W. and R.P. Archer, *An investigation of the psychometric properties of the MMPI-2 Restructured Clinical (RC) scales with mental health inpatients.* J Pers Assess, 2008. **90**(3): p. 239-49.

461. Handel, R.W., et al., *Psychometric functioning of the MMPI-2-RF VRIN-r and TRIN-r scales with varying degrees of randomness, acquiescence, and counter-acquiescence.* Psychol Assess, 2010. **22**(1): p. 87-95.

462. Hoelzle, J.B. and G.J. Meyer, *The invariant component structure of the Personality Assessment Inventory (PAI) full scales.* J Pers Assess, 2009. **91**(2): p. 175-86.

463. McCredie, M.N. and L.C. Morey, *Evaluating new supplemental indicators for the Personality Assessment Inventory: Standardization and cross-validation.* Psychol Assess, 2018. **30**(10): p. 1292-1299.

464. Morey, L.C. and C.J. Hopwood, *Efficiency of a strategy for detecting back random responding on the personality assessment inventory.* Psychol Assess, 2004. **16**(2): p. 197-200.

465. Ruiz, M.A. and J.F. Edens, *Recovery and replication of internalizing and externalizing dimensions within the personality assessment inventory.* J Pers Assess, 2008. **90**(6): p. 585-92.

466. Siefert, C.J., et al., *An item-level psychometric analysis of the personality assessment inventory: clinical scales in a psychiatric inpatient unit.* Assessment, 2009. **16**(4): p. 373-83.

467. Slavin-Mulford, J., et al., *External validity of the personality assessment inventory (PAI) in a clinical sample.* J Pers Assess, 2012. **94**(6): p. 593-600.

468. Whiteside, D., et al., *Relationship between suboptimal cognitive effort and the clinical scales of the Personality Assessment Inventory.* Clin Neuropsychol, 2010. **24**(2): p. 315-25.

Copyright ©2021 Reed Group, Ltd.

469. Ortiz-Tallo, M., et al., *Personalidad y síndromes clínicos: un estudio con el MCMI-III basado en una muestra española.* Revista de psicopatología y psicología clínica, 2011. **16**(1): p. 49-59.

470. Aaronson, A.L., O.B. Dent, and C.D. Kline, *Cross-validation of MMPI and MMPI-2 predictor scales.* J Clin Psychol, 1996. **52**(3): p. 311-5.

471. Ben-Porath, Y.S. and J.N. Butcher, *The comparability of MMPI and MMPI-2 scales and profiles.* Psychological Assessment: A Journal of Consulting and Clinical Psychology, 1989. **1**(4): p. 345-347.

472. Butcher, J.N. and J.R. Graham, *The MMPI-2: A new standard for personality assessment and research in counseling settings.* Measurement and Evaluation in Counseling and Development, 1994. **27**(3): p. 131-150.

473. Pollack, D.R. and T.F. Grainey, *A comparison of MMPI profiles for state and private disability insurance applicants.* J Pers Assess, 1984. **48**(2): p. 121-5.

474. A. Weiss, P., K. J. Bell, and W. U. Weiss, *Use of the MMPI-2 Restructured Clinical (RC) Scales in Detecting Criminal Malingering*. Vol. 25. 2010. 49-55.

475. Braxton, L.E., et al., *Validity rates of the Personality Assessment Inventory and the Minnesota Multiphasic Personality Inventory-2 in a VA Medical Center Setting.* J Pers Assess, 2007. **88**(1): p. 5-15.

476. Deisinger, J., *Exploring the factor structure of the Personality Assessment Inventory*. Vol. 2. 1995. 173-179.

477. Morey, L.C., et al., *Personality Assessment Inventory profiles of deployed combat troops: an empirical investigation of normative performance.* Psychol Assess, 2011. **23**(2): p. 456-62.

478. Brown, K.P., R.J. Iannelli, and D.P. Marganoff, *Use of the Personality Assessment Inventory in Fitness-for-Duty Evaluations of Physicians.* J Pers Assess, 2017. **99**(5): p. 465-471.

479. Alexy, W.D. and P.M. Webb, *Utility of the MMPI-2 in Work-Hardening rehabilitation.* Rehabilitation Psychology, 1999. **44**(3): p. 266-273.

480. Meyers, J.E., S.R. Millis, and K. Volkert, *A validity index for the MMPI-2.* Arch Clin Neuropsychol, 2002. **17**(2): p. 157-69.

481. Arbisi, P.A., *Use of the MMPI-2 in Personal Injury and Disability Evaluations*, in *MMPI-2: A practitioner's guide.* 2006, American Psychological Association: Washington, DC, US. p. 407-441.

482. Colotla, V.A., M.L. Bowman, and R.J. Shercliffe, *Test-retest stability of injured workers' MMPI-2 profiles.* Psychol Assess, 2001. **13**(4): p. 572-6.

483. Fox, D.D., A. Gerson, and P.R. Lees-Haley, *Interrelationship of MMPI-2 validity scales in personal injury claims.* J Clin Psychol, 1995. **51**(1): p. 42-7.

484. Gervais, R.O., et al., *Development and validation of a Response Bias Scale (RBS) for the MMPI-2.* Assessment, 2007. **14**(2): p. 196-208.

485. Henry, G.K., et al., *The Henry-Heilbronner Index: a 15-item empirically derived MMPI-2 subscale for identifying probable malingering in personal injury litigants and disability claimants.* Clin Neuropsychol, 2006. **20**(4): p. 786-97.

486. Lees-Haley, P.R., *MMPI—2 F and F-K scores of personal injury malingerers in vocational neuropsychological and emotional distress claims.* American Journal of Forensic Psychology, 1991. **9**(3): p. 5-14.

487. Livingston, R.B., et al., *MMPI--2 Code-Type Congruence of Injured Workers.* Psychol Assess, 2006. **18**(1): p. 126-30.

488. Nelson, N.W., J.J. Sweet, and R.L. Heilbronner, *Examination of the new MMPI-2 Response Bias Scale (Gervais): relationship with MMPI-2 validity scales.* J Clin Exp Neuropsychol, 2007. **29**(1): p. 67-72.

Copyright ©2021 Reed Group, Ltd.

489. Yoxall, J., M. Bahr, and T. O'Neill, *Faking bad in workers compensation psychological assessments: Elevation rates of negative distortion scales on the personality assessment inventory in an Australian sample.* Psychiatry, Psychology and Law, 2017. **24**(5): p. 682-693.

490. Schutte, J.W., *Using the MCMI-III in forensic evaluations*. Vol. 19. 2001. 5-20.

491. Wygant, D.B., et al., *Further validation of the MMPI-2 and MMPI-2-RF Response Bias Scale: findings from disability and criminal forensic settings.* Psychol Assess, 2010. **22**(4): p. 745-56.

492. Douglas, K.S., S.D. Hart, and P.R. Kropp, *Validity of the Personality Assessment Inventory for forensic assessments.* International Journal of Offender Therapy and Comparative Criminology, 2001. **45**(2): p. 183-197.

493. Morey, L.C., M.B. Warner, and C.J. Hopwood, *The Personality Assessment Inventory: Issues in Legal and Forensic Settings*, in *Forensic psychology: Emerging topics and expanding roles.* 2007, John Wiley & Sons Inc: Hoboken, NJ, US. p. 97-126.

494. Mullen, K.L. and J.F. Edens, *A case law survey of the Personality Assessment Inventory: examining its role in civil and criminal trials.* J Pers Assess, 2008. **90**(3): p. 300-3.

495. Douglas, K.S., et al., *The Personality Assessment Inventory as a proxy for the Psychopathy Checklist Revised: testing the incremental validity and cross-sample robustness of the Antisocial Features Scale.* Assessment, 2007. **14**(3): p. 255-69.

496. Kucharski, L.T., et al., *The Utility of the Personality Assessment Inventory in the Assessment of Psychopathy.* Journal of Forensic Psychology Practice, 2008. **8**(4): p. 344-357.

497. Rogers, R., K.L. Ustad, and R.T. Salekin, *Convergent validity of the personality assessment inventory: A study of emergency referrals in a correctional setting.* Assessment, 1998. **5**(1): p. 3-12.

498. Baer, R.A., et al., *Sensitivity of MMPI-2 validity scales to underreporting of symptoms.* Psychological Assessment, 1995. **7**(4): p. 419-423.

499. Baer, R.A. and G. Sekirnjak, *Detection of underreporting on the MMPI-2 in a clinical population: effects of information about validity scales.* J Pers Assess, 1997. **69**(3): p. 555-67.

500. Baer, R.A. and J. Miller, *Underreporting of psychopathology on the MMPI-2: a meta-analytic review.* Psychol Assess, 2002. **14**(1): p. 16-26.

501. Bagby, R.M., et al., *Detecting feigned depression and schizophrenia on the MMPI-2.* J Pers Assess, 1997. **68**(3): p. 650-64.

502. Burchett, D.L. and Y.S. Ben-Porath, *The impact of overreporting on MMPI-2-RF substantive scale score validity.* Assessment, 2010. **17**(4): p. 497-516.

503. Crighton, A.H., et al., *Utility of the MMPI-2-RF Validity Scales in Detection of Simulated Underreporting: Implications of Incorporating a Manipulation Check.* Assessment, 2017. **24**(7): p. 853-864.

504. Sellbom, M. and R.M. Bagby, *Validity of the MMPI-2-RF (restructured form) L-r and K-r scales in detecting underreporting in clinical and nonclinical samples.* Psychol Assess, 2008. **20**(4): p. 370-6.

505. Sellbom, M. and R.M. Bagby, *Detection of overreported psychopathology with the MMPI-2-RF [corrected] validity scales.* Psychol Assess, 2010. **22**(4): p. 757-67.

506. Timbrook, R.E., et al., *Comparison of the Wiener-Harmon Subtle-Obvious scales and the standard validity scales in detecting valid and invalid MMPI-2 profiles.* Psychological Assessment, 1993. **5**(1): p. 53.

507. Walters, G.L. and J.R. Clopton, *Effect of symptom information and validity scale information on the malingering of depression on the MMPI-2.* J Pers Assess, 2000. **75**(2): p. 183-99.

Copyright ©2021 Reed Group, Ltd.

508. Hawes, S.W. and M.T. Boccaccini, *Detection of overreporting of psychopathology on the Personality Assessment Inventory: a meta-analytic review.* Psychol Assess, 2009. **21**(1): p. 112-24.

509. Hopwood, C.J., et al., *Malingering on the Personality Assessment Inventory: Identification of Specific Feigned Disorders.* Journal of Personality Assessment, 2007. **88**(1): p. 43-48.

510. Griffiths, K.M., et al., *Effect of web-based depression literacy and cognitive–behavioural therapy interventions on stigmatising attitudes to depression: Randomised controlled trial.* The British Journal of Psychiatry, 2004. **185**(4): p. 342-349.

511. Hovens, J., et al., *The assessment of posttraumatic stress disorder: with the Clinician Administered PTSD Scale: Dutch results.* Journal of clinical psychology, 1994. **50**(3): p. 325-340.

512. Hyer, L., et al., *Assessment of older combat veterans with the clinician-administered PTSD scale.* J Trauma Stress, 1996. **9**(3): p. 587-93.

513. Piersma, H.L., *The MCMI-II depression scales: do they assist in the differential prediction of depressive disorders?* Journal of personality assessment, 1991. **56**(3): p. 478-486.

514. Olsen, A.M. and C.O. Veltri, *The moderating influence of disorder on coached overreporting using the MMPI-2-RF.* Journal of personality assessment, 2018.

515. Benitez, J., et al., *The clinical validity and utility of combinatorial pharmacogenomics: Enhancing patient outcomes.* Applied & translational genomics, 2015. **5**: p. 47-49.

516. Brennan, F.X., et al., *A naturalistic study of the effectiveness of pharmacogenetic testing to guide treatment in psychiatric patients with mood and anxiety disorders.* The primary care companion for CNS disorders, 2015. **17**(2).

517. Olson, M., et al., *Clinical Impact of Pharmacogenetic-Guided Treatment for Patients Exhibiting Neuropsychiatric Disorders: A Randomized Controlled Trial.* The primary care companion for CNS disorders, 2017. **19**(2).

518. Ontario, H.Q., *Pharmacogenomic testing for psychotropic medication selection: a systematic review of the Assurex GeneSight Psychotropic Test.* Ontario health technology assessment series, 2017. **17**(4): p. 1.

519. Steimer, W., et al., *Pharmacogenetics: a new diagnostic tool in the management of antidepressive drug therapy.* Clinica Chimica Acta, 2001. **308**(1-2): p. 33-41.

520. Winner, J., et al., *Psychiatric pharmacogenomics predicts health resource utilization of outpatients with anxiety and depression.* Translational psychiatry, 2013. **3**(3): p. e242.

521. Bradley, P., et al., *Improved efficacy with targeted pharmacogenetic-guided treatment of patients with depression and anxiety: a randomized clinical trial demonstrating clinical utility.* Journal of psychiatric research, 2018. **96**: p. 100-107.

522. Merom, D., et al., *Promoting walking as an adjunct intervention to group cognitive behavioral therapy for anxiety disorders—a pilot group randomized trial.* Journal of anxiety disorders, 2008. **22**(6): p. 959-968.

523. Heimberg, R.G., et al., *Cognitive behavioral group therapy vs phenelzine therapy for social phobia: 12-week outcome.* Archives of General Psychiatry, 1998. **55**(12): p. 1133-1141.

524. Broocks, A., et al., *Comparison of aerobic exercise, clomipramine, and placebo in the treatment of panic disorder.* American Journal of Psychiatry, 1998. **155**(5): p. 603-609.

525. Katula, J.A., B.J. Blissmer, and E. McAuley, *Exercise intensity and self-efficacy effects on anxiety reduction in healthy, older adults.* Journal of Behavioral Medicine, 1999. **22**(3): p. 233-247.

526. Parente, D., *Influence of aerobic and stretching exercise on anxiety and sensation-seeking mood state.* Perceptual and Motor Skills, 2000. **90**(1): p. 347-348.

Copyright ©2021 Reed Group, Ltd.

527. Watanabe, E., et al., *Comparison of water-and land-based exercise in the reduction of state anxiety among older adults.* Perceptual and motor skills, 2000. **91**(1): p. 97-104.

528. Marquez, D.X., et al., *Self-efficacy manipulation and state anxiety responses to exercise in low active women.* Psychology and Health, 2002. **17**(6): p. 783-791.

529. McAuley, E., et al., *Physical activity and physique anxiety in older adults: fitness, and efficacy influences.* Aging & mental health, 2002. **6**(3): p. 222-230.

530. Broman-Fulks, J.J. and K.M. Storey, *Evaluation of a brief aerobic exercise intervention for high anxiety sensitivity.* Anxiety, Stress, & Coping, 2008. **21**(2): p. 117-128.

531. Martinsen, E.W., *Physical activity in the prevention and treatment of anxiety and depression.* Nordic journal of psychiatry, 2008. **62**(sup47): p. 25-29.

532. Phongsavan, P., et al., *Process evaluation in an intervention designed to promote physical activity among adults with anxiety disorders: evidence of acceptability and adherence.* Health Promotion Journal of Australia, 2008. **19**(2): p. 137-143.

533. Smits, J.A., et al., *Reducing anxiety sensitivity with exercise.* Depression and anxiety, 2008. **25**(8): p. 689-699.

534. Knapen, J., et al., *State anxiety and subjective well-being responses to acute bouts of aerobic exercise in patients with depressive and anxiety disorders.* British Journal of Sports Medicine, 2009. **43**(10): p. 756-759.

535. Bibeau, W.S., et al., *Effects of acute resistance training of different intensities and rest periods on anxiety and affect.* The Journal of Strength & Conditioning Research, 2010. **24**(8): p. 2184-2191.

536. Herring, M.P., P.J. O'connor, and R.K. Dishman, *The effect of exercise training on anxiety symptoms among patients: a systematic review.* Archives of internal medicine, 2010. **170**(4): p. 321-331.

537. Musalek, M., et al., *Psychopathology in the 21st century.* The World Journal of Biological Psychiatry, 2010. **11**(7): p. 844-851.

538. Carraro, A. and E. Gobbi, *Effects of an exercise programme on anxiety in adults with intellectual disabilities.* Research in developmental disabilities, 2012. **33**(4): p. 1221-1226.

539. Herring, M.P., et al., *Feasibility of exercise training for the short-term treatment of generalized anxiety disorder: a randomized controlled trial.* Psychotherapy and psychosomatics, 2012. **81**(1): p. 21-28.

540. Jazaieri, H., et al., *A randomized trial of MBSR versus aerobic exercise for social anxiety disorder.* Journal of clinical psychology, 2012. **68**(7): p. 715-731.

541. Bartley, C.A., M. Hay, and M.H. Bloch, *Meta-analysis: aerobic exercise for the treatment of anxiety disorders.* Progress in Neuro-Psychopharmacology and Biological Psychiatry, 2013. **45**: p. 34-39.

542. Hovland, A., et al., *Comparing physical exercise in groups to group cognitive behaviour therapy for the treatment of panic disorder in a randomized controlled trial.* Behavioural and cognitive psychotherapy, 2013. **41**(4): p. 408-432.

543. Jayakody, K., S. Gunadasa, and C. Hosker, *Exercise for anxiety disorders: systematic review.* Br J Sports Med, 2014. **48**(3): p. 187-196.

544. Wang, C.-W., et al., *Managing stress and anxiety through qigong exercise in healthy adults: a systematic review and meta-analysis of randomized controlled trials.* BMC complementary and alternative medicine, 2014. **14**(1): p. 8.

545. Broman-Fulks, J.J., K. Kelso, and L. Zawilinski, *Effects of a single bout of aerobic exercise versus resistance training on cognitive vulnerabilities for anxiety disorders.* Cognitive behaviour therapy, 2015. **44**(4): p. 240-251.

Copyright ©2021 Reed Group, Ltd.

546. Ensari, I., et al., *Meta-analysis of acute exercise effects on state anxiety: an update of randomized controlled trials over the past 25 years.* Depression and anxiety, 2015. **32**(8): p. 624-634.

547. Gaudlitz, K., et al., *Aerobic exercise training facilitates the effectiveness of cognitive behavioral therapy in panic disorder.* Depression and anxiety, 2015. **32**(3): p. 221-228.

548. LeBouthillier, D.M. and G.J. Asmundson, *A single bout of aerobic exercise reduces anxiety sensitivity but not intolerance of uncertainty or distress tolerance: A randomized controlled trial.* Cognitive behaviour therapy, 2015. **44**(4): p. 252-263.

549. Chen, H.-M., H.-H. Wang, and M.-H. Chiu, *Effectiveness of a releasing exercise program on anxiety and self-efficacy among nurses.* Western journal of nursing research, 2016. **38**(2): p. 169-182.

550. Herring, M.P., K.E. Johnson, and P.J. O'connor, *Exercise training and health-related quality of life in generalized anxiety disorder.* Psychology of sport and exercise, 2016. **27**: p. 138-141.

551. Jazaieri, H., et al., *Pre-treatment social anxiety severity moderates the impact of mindfulness-based stress reduction and aerobic exercise.* Psychology and Psychotherapy: Theory, Research and Practice, 2016. **89**(2): p. 229-234.

552. Mochcovitch, M.D., et al., *The effects of regular physical activity on anxiety symptoms in healthy older adults: a systematic review.* Revista Brasileira de Psiquiatria, 2016. **38**(3): p. 255-261.

553. Sabourin, B.C., et al., *Two Interventions Decrease Anxiety Sensitivity Among High Anxiety Sensitive Women: Could Physical Exercise Be the Key?* Journal of Cognitive Psychotherapy, 2016. **30**(2): p. 131-146.

554. Edwards, M.K., R.E. Rhodes, and P.D. Loprinzi, *A randomized control intervention investigating the effects of acute exercise on emotional regulation.* American journal of health behavior, 2017. **41**(5): p. 534-543.

555. Gordon, B.R., et al., *The effects of resistance exercise training on anxiety: a meta-analysis and meta-regression analysis of randomized controlled trials.* Sports Medicine, 2017. **47**(12): p. 2521-2532.

556. Kutty, N.A.M., M.A.R. Jabbar, and Y.S. Ving, *Effects of Trampoline Exercise on Attentional Control and Daytime Sleepiness among Young Adults with Anxiety Disorders in Malaysia.* Disability, CBR & Inclusive Development, 2017. **28**(4): p. 96-109.

557. Ma, W.-F., et al., *The Effects of an Exercise Program on Anxiety Levels and Metabolic Functions in Patients With Anxiety Disorders.* Biological research for nursing, 2017. **19**(3): p. 258-268.

558. Stubbs, B., et al., *An examination of the anxiolytic effects of exercise for people with anxiety and stress-related disorders: A meta-analysis.* Psychiatry Research, 2017. **249**: p. 102-108.

559. Aguiñaga, S., et al., *Home-based physical activity program improves depression and anxiety in older adults.* Journal of physical activity and health, 2018. **15**(9): p. 692-696.

560. Albracht-Schulte, K. and J. Robert-McComb, *The effects of yoga and quiet rest on subjective levels of anxiety and physiological correlates: a 2-way crossover randomized trial.* BMC complementary and alternative medicine, 2018. **18**(1): p. 280.

561. Aylett, E., N. Small, and P. Bower, *Exercise in the treatment of clinical anxiety in general practice–a systematic review and meta-analysis.* BMC health services research, 2018. **18**(1): p. 559.

562. Blough, J. and P.D. Loprinzi, *Experimentally investigating the joint effects of physical activity and sedentary behavior on depression and anxiety: A randomized controlled trial.* Journal of affective disorders, 2018. **239**: p. 258-268.

563. Lattari, E., et al., *Effects of aerobic exercise on anxiety symptoms and cortical activity in patients with panic disorder: a pilot study.* Clinical practice and epidemiology in mental health: CP & EMH, 2018. **14**: p. 11.

Copyright ©2021 Reed Group, Ltd.

564. Lucibello, K., J. Parker, and J. Heisz, *Examining a training effect on the state anxiety response to an acute bout of exercise in low and high anxious individuals.* Journal of affective disorders, 2019. **247**: p. 29-35.

565. Bischoff, S., et al., *Running for extinction? Aerobic exercise as an augmentation of exposure therapy in panic disorder with agoraphobia.* Journal of psychiatric research, 2018. **101**: p. 34-41.

566. Lambert, R.A., I. Harvey, and F. Poland, *A pragmatic, unblinded randomised controlled trial comparing an occupational therapy-led lifestyle approach and routine GP care for panic disorder treatment in primary care.* J Affect Disord, 2007. **99**(1-3): p. 63-71.

567. Martinsen, E.W., A. Hoffart, and Ø.Y. Solberg, *Aerobic and non-aerobic forms of exercise in the treatment of anxiety disorders.* Stress Medicine, 1989. **5**(2): p. 115-120.

568. Oeland, A.-M., et al., *Impact of exercise on patients with depression and anxiety.* Nordic journal of psychiatry, 2010. **64**(3): p. 210-217.

569. Sexton, H., A. Maere, and N.H. Dahl, *Exercise intensity and reduction in neurotic symptoms. A controlled follow-up study.* Acta Psychiatr Scand, 1989. **80**(3): p. 231-5.

570. Wedekind, D., et al., *A randomized, controlled trial of aerobic exercise in combination with paroxetine in the treatment of panic disorder.* The World Journal of Biological Psychiatry, 2010. **11**(7): p. 904-913.

571. Esquivel, G., et al., *Acute exercise reduces the effects of a 35% CO2 challenge in patients with panic disorder.* J Affect Disord, 2008. **107**(1-3): p. 217-20.

572. Kirkwood, G., et al., *Yoga for anxiety: a systematic review of the research evidence.* British journal of sports medicine, 2005. **39**(12): p. 884-891.

573. Krisanaprakornkit, T., et al., *Meditation therapy for anxiety disorders.* Cochrane Database of Systematic Reviews, 2006(1).

574. Koszycki, D., et al., *Randomized trial of a meditation-based stress reduction program and cognitive behavior therapy in generalized social anxiety disorder.* Behaviour Research and Therapy, 2007. **45**(10): p. 2518-2526.

575. Goldin, P., et al., *Randomized controlled trial of mindfulness-based stress reduction versus aerobic exercise: effects on the self-referential brain network in social anxiety disorder.* Frontiers in human neuroscience, 2012. **6**: p. 295.

576. Chugh-Gupta, N., F.G. Baldassarre, and B.H. Vrkljan, *A systematic review of yoga for state anxiety: Considerations for occupational therapy/Revue systématique sur l'efficacité du yoga pour traiter l'anxiété réactionnelle: Facteurs à considérer en ergothérapie.* Canadian Journal of Occupational Therapy, 2013. **80**(3): p. 150-170.

577. Hoge, E.A., et al., *Randomized controlled trial of mindfulness meditation for generalized anxiety disorder: effects on anxiety and stress reactivity.* The Journal of clinical psychiatry, 2013. **74**(8): p. 786.

578. Sharma, M. and T. Haider, *Yoga as an alternative and complementary therapy for patients suffering from anxiety: A systematic review.* Journal of Evidence-Based Complementary & Alternative Medicine, 2013. **18**(1): p. 15-22.

579. Chu, A., et al., *Do workplace physical activity interventions improve mental health outcomes?* Occupational Medicine, 2014. **64**(4): p. 235-245.

580. Vorkapic, C.F. and B. Rangé, *Reducing the symptomatology of panic disorder: the effects of a yoga program alone and in combination with cognitive-behavioral therapy.* Frontiers in psychiatry, 2014. **5**: p. 177.

581. Hofmann, S.G., et al., *Yoga for generalized anxiety disorder: design of a randomized controlled clinical trial.* Contemporary clinical trials, 2015. **44**: p. 70-76.

Copyright ©2021 Reed Group, Ltd.

582. Hofmann, S.G., et al., *Effect of Hatha yoga on anxiety: a meta-analysis.* Journal of Evidence-Based Medicine, 2016. **9**(3): p. 116-124.

583. Cramer, H., et al., *Yoga for anxiety: A systematic review and meta-analysis of randomized controlled trials.* Depression and anxiety, 2018. **35**(9): p. 830-843.

584. Uebelacker, L.A. and M.K. Broughton, *Yoga for Depression and Anxiety: A Review of Published Research and Implications for Healthcare Providers.* Focus, 2018. **16**(1): p. 95-97.

585. Vollbehr, N.K., et al., *Hatha yoga for acute, chronic and/or treatment-resistant mood and anxiety disorders: A systematic review and meta-analysis.* PloS one, 2018. **13**(10): p. e0204925.

586. Anderson, N., et al., *Faith-adapted psychological therapies for depression and anxiety: Systematic review and meta-analysis.* Journal of Affective Disorders, 2015. **176**: p. 183-196.

587. Arntz, A. and M. Van Den Hout, *Psychological treatments of panic disorder without agoraphobia: Cognitive therapy versus applied relaxation.* Behaviour Research and Therapy, 1996. **34**(2): p. 113-121.

588. ATAOĞLU, A., et al., *Alprazolam and cognitive behavior therapy in treatment of panic disorder.* Turkish Journal of Medical Sciences, 2000. **30**(2): p. 167-172.

589. Bados, A., G. Balaguer, and C. Saldaña, *Outcome of cognitive-behavioural therapy in training practice with anxiety disorder patients.* British Journal of Clinical Psychology, 2007. **46**(4): p. 429-435.

590. Bakker, A., et al., *Cognitive therapy by allocation versus cognitive therapy by preference in the treatment of panic disorder.* Psychotherapy and psychosomatics, 2000. **69**(5): p. 240-243.

591. Barlow, D.H., et al., *Cognitive-behavioral therapy, imipramine, or their combination for panic disorder: A randomized controlled trial.* Jama, 2000. **283**(19): p. 2529-2536.

592. Bergström, J., et al., *Internet-versus group-administered cognitive behaviour therapy for panic disorder in a psychiatric setting: a randomised trial.* BMC psychiatry, 2010. **10**(1): p. 54.

593. Blanco, C., et al., *A placebo-controlled trial of phenelzine, cognitive behavioral group therapy, and their combination for social anxiety disorder.* Archives of General Psychiatry, 2010. **67**(3): p. 286-295.

594. Bohni, M., et al., *A randomized study of massed three-week cognitive behavioural therapy schedule for panic disorder.* Acta Psychiatrica Scandinavica, 2009. **120**(3): p. 187-195.

595. Borgeat, F., et al., *Does the form or the amount of exposure make a difference in the cognitive-behavioral therapy treatment of social phobia?* The Journal of nervous and mental disease, 2009. **197**(7): p. 507-513.

596. Brenes, G.A., et al., *Telephone-delivered cognitive behavioral therapy and telephone-delivered nondirective supportive therapy for rural older adults with generalized anxiety disorder: a randomized clinical trial.* JAMA psychiatry, 2015. **72**(10): p. 1012-1020.

597. Brenes, G.A., et al., *A randomized controlled trial of telephone-delivered cognitive-behavioral therapy for late-life anxiety disorders.* The American Journal of Geriatric Psychiatry, 2012. **20**(8): p. 707-716.

598. Brown, G.K., et al., *A comparison of focused and standard cognitive therapy for panic disorder.* Journal of Anxiety Disorders, 1997. **11**(3): p. 329-345.

599. Butler, G., et al., *Comparison of behavior therapy and cognitive behavior therapy in the treatment of generalized anxiety disorder.* Journal of consulting and clinical psychology, 1991. **59**(1): p. 167.

600. Carlbring, P., et al., *Treatment of panic disorder: live therapy vs. self-help via the Internet.* Behaviour research and therapy, 2005. **43**(10): p. 1321-1333.

Copyright ©2021 Reed Group, Ltd.

601. Carpenter, J.K., et al., *Cognitive behavioral therapy for anxiety and related disorders: A meta-analysis of randomized placebo-controlled trials.* Depression and anxiety, 2018. **35**(6): p. 502-514.

602. Christensen, H., et al., *A comparison of changes in anxiety and depression symptoms of spontaneous users and trial participants of a cognitive behavior therapy website.* Journal of medical Internet research, 2004. **6**(4): p. e46.

603. Clark, D.M., et al., *Cognitive therapy versus exposure and applied relaxation in social phobia: A randomized controlled trial.* Journal of consulting and clinical psychology, 2006. **74**(3): p. 568.

604. Clond, M., *Emotional freedom techniques for anxiety: a systematic review with meta-analysis.* The Journal of nervous and mental disease, 2016. **204**(5): p. 388-395.

605. Cooper, K., et al., *Cognitive behaviour therapy for health anxiety: a systematic review and meta-analysis.* Behavioural and cognitive psychotherapy, 2017. **45**(2): p. 110-123.

606. Cottraux, J., et al., *Cognitive behavior therapy versus supportive therapy in social phobia: a randomized controlled trial.* Psychotherapy and Psychosomatics, 2000. **69**(3): p. 137-146.

607. Coull, G. and P. Morris, *The clinical effectiveness of CBT-based guided self-help interventions for anxiety and depressive disorders: a systematic review.* Psychological medicine, 2011. **41**(11): p. 2239-2252.

608. Craske, M.G., et al., *Cognitive behavioral therapy for panic disorder and comorbidity: more of the same or less of more?* Behaviour Research and Therapy, 2007. **45**(6): p. 1095-1109.

609. Craske, M.G., et al., *Does the addition of cognitive behavioral therapy improve panic disorder treatment outcome relative to medication alone in the primary-care setting?* Psychological Medicine, 2005. **35**(11): p. 1645-1654.

610. Craske, M.G., E. Maidenberg, and A. Bystritsky, *Brief cognitive-behavioral versus nondirective therapy for panic disorder.* Journal of Behavior Therapy and Experimental Psychiatry, 1995. **26**(2): p. 113-120.

611. Cuijpers, P., et al., *Relative effects of cognitive and behavioral therapies on generalized anxiety disorder, social anxiety disorder and panic disorder: A meta-analysis.* Journal of Anxiety Disorders, 2016. **43**: p. 79-89.

612. Dannon, P.N., et al., *Cognitive behavioral group therapy in panic disorder patients: the efficacy of CBGT versus drug treatment.* Annals of Clinical Psychiatry, 2004. **16**(1): p. 41-46.

613. De Oliveira, I., et al., *Efficacy of the trial-based thought record, a new cognitive therapy strategy designed to change core beliefs, in social phobia.* Journal of clinical pharmacy and therapeutics, 2012. **37**(3): p. 328-334.

614. Deshmukh, V.M., et al., *Anxiety, panic and adult asthma: a cognitive-behavioral perspective.* Respiratory Medicine, 2007. **101**(2): p. 194-202.

615. DiNapoli, E.A., et al., *Effects of home-delivered cognitive behavioral therapy (CBT) for depression on anxiety symptoms among rural, ethnically diverse older adults.* Clinical gerontologist, 2017. **40**(3): p. 181-190.

616. Ezegbe, B.N., et al., *Impacts of cognitive-behavioral intervention on anxiety and depression among social science education students: A randomized controlled trial.* Medicine, 2019. **98**(15).

617. Farvolden, P., et al., *Usage and longitudinal effectiveness of a Web-based self-help cognitive behavioral therapy program for panic disorder.* Journal of medical Internet research, 2005. **7**(1): p. e7.

618. Freedman, S. and R. Adessky, *Cognitive behavior therapy for panic disorder.* Israel Journal of Psychiatry and Related Sciences, 2009. **46**(4): p. 251.

619. Freire, R.C., et al., *Treatment–resistant panic disorder: a systematic review.* Expert opinion on pharmacotherapy, 2016. **17**(2): p. 159-168.

Copyright ©2021 Reed Group, Ltd.

620. Furukawa, T.A., N. Watanabe, and R. Churchill, *Combined psychotherapy plus antidepressants for panic disorder with or without agoraphobia.* Cochrane Database of Systematic Reviews, 2007(1).

621. Gallagher, M.W., et al., *Mechanisms of change in cognitive behavioral therapy for panic disorder: The unique effects of self-efficacy and anxiety sensitivity.* Behaviour research and therapy, 2013. **51**(11): p. 767-777.

622. Gloster, A.T., et al., *Long-term stability of cognitive behavioral therapy effects for panic disorder with agoraphobia: a two-year follow-up study.* Behaviour research and therapy, 2013. **51**(12): p. 830-839.

623. Gloster, A.T., et al., *Psychological treatment for panic disorder with agoraphobia: a randomized controlled trial to examine the role of therapist-guided exposure in situ in CBT.* Journal of consulting and clinical psychology, 2011. **79**(3): p. 406.

624. Goldin, P.R., et al., *Group CBT versus MBSR for social anxiety disorder: A randomized controlled trial.* Journal of Consulting and Clinical Psychology, 2016. **84**(5): p. 427.

625. Goldin, P.R., et al., *Impact of cognitive-behavioral therapy for social anxiety disorder on the neural bases of emotional reactivity to and regulation of social evaluation.* Behaviour research and therapy, 2014. **62**: p. 97-106.

626. Gould, R.L., M.C. Coulson, and R.J. Howard, *Efficacy of cognitive behavioral therapy for anxiety disorders in older people: A meta-analysis and meta-regression of randomized controlled trials.* Journal of the American Geriatrics Society, 2012. **60**(2): p. 218-229.

627. Härtling, S., et al., *Cognitive therapy and task concentration training applied as intensified group therapies for social anxiety disorder with fear of blushing—A randomized controlled trial.* Clinical psychology & psychotherapy, 2016. **23**(6): p. 509-522.

628. Haug, T., et al., *Stepped care versus face-to–face cognitive behavior therapy for panic disorder and social anxiety disorder: predictors and moderators of outcome.* Behaviour research and therapy, 2015. **71**: p. 76-89.

629. Hedman, E., et al., *Cost-effectiveness and long-term effectiveness of internet-based cognitive behaviour therapy for severe health anxiety.* Psychological medicine, 2013. **43**(2): p. 363-374.

630. Helmes, E. and B.G. Ward, *Mindfulness-based cognitive therapy for anxiety symptoms in older adults in residential care.* Aging & mental health, 2017. **21**(3): p. 272-278.

631. Hendriks, G., et al., *Cognitive-behavioural therapy for late-life anxiety disorders: a systematic review and meta-analysis.* Acta Psychiatrica Scandinavica, 2008. **117**(6): p. 403-411.

632. Hendriks, G.J., et al., *A randomized controlled study of paroxetine and cognitive-behavioural therapy for late-life panic disorder.* Acta Psychiatrica Scandinavica, 2010. **122**(1): p. 11-19.

633. Hicks, T.V., et al., *Physical, mental, and social catastrophic cognitions as prognostic factors in cognitive-behavioral and pharmacological treatments for panic disorder.* Journal of Consulting and Clinical Psychology, 2005. **73**(3): p. 506.

634. Hoffart, A., et al., *Cognitive and guided mastery therapies for panic disorder with agoraphobia: 18-year long-term outcome and predictors of long-term change.* Clinical psychology & psychotherapy, 2016. **23**(1): p. 1-13.

635. Hoyer, J., et al., *Manualized cognitive therapy versus cognitive-behavioral treatment-as-usual for social anxiety disorder in routine practice: A cluster-randomized controlled trial.* Behaviour research and therapy, 2017. **95**: p. 87-98.

636. Huppert, J.D., et al., *Therapists, therapist variables, and cognitive-behavioral therapy outcome in a multicenter trial for panic disorder.* Journal of consulting and clinical psychology, 2001. **69**(5): p. 747.

637. Kenardy, J., et al., *A comparison of delivery methods of cognitive-behavioral therapy for panic disorder: an international multicenter trial.* Journal of consulting and clinical psychology, 2003. **71**.

Copyright ©2021 Reed Group, Ltd.

638. Kim, Y.W., et al., *Effectiveness of mindfulness-based cognitive therapy as an adjuvant to pharmacotherapy in patients with panic disorder or generalized anxiety disorder.* Depression and anxiety, 2009. **26**(7): p. 601-606.

639. King, A.L.S., et al., *Efficacy of a specific model for cognitive-behavioral therapy among panic disorder patients with agoraphobia: a randomized clinical trial.* São Paulo medical journal, 2011. **129**(5): p. 325-334.

640. Kircher, T., et al., *Effect of cognitive-behavioral therapy on neural correlates of fear conditioning in panic disorder.* Biological Psychiatry, 2013. **73**(1): p. 93-101.

641. Kiropoulos, L.A., et al., *Is internet-based CBT for panic disorder and agoraphobia as effective as face-to-face CBT?* Journal of anxiety disorders, 2008. **22**(8): p. 1273-1284.

642. Leichsenring D Sc, F., et al., *Short-term psychodynamic psychotherapy and cognitive-behavioral therapy in generalized anxiety disorder: a randomized, controlled trial.* American Journal of Psychiatry, 2009. **166**(8): p. 875-881.

643. Leichsenring, F., et al., *Psychodynamic therapy and cognitive-behavioral therapy in social anxiety disorder: a multicenter randomized controlled trial.* American Journal of Psychiatry, 2013. **170**(7): p. 759-767.

644. Marchand, A., et al., *A randomized, controlled clinical trial of standard, group and brief cognitive-behavioral therapy for panic disorder with agoraphobia: a two-year follow-up.* Journal of Anxiety Disorders, 2009. **23**(8): p. 1139-1147.

645. Mayo-Wilson, E. and P. Montgomery, *Media-delivered cognitive behavioural therapy and behavioural therapy (self-help) for anxiety disorders in adults.* Cochrane Database of Systematic Reviews, 2013(9).

646. McManus, F., et al., *A randomized clinical trial of mindfulness-based cognitive therapy versus unrestricted services for health anxiety (hypochondriasis).* Journal of consulting and clinical psychology, 2012. **80**(5): p. 817.

647. Montero-Marin, J., et al., *Is cognitive–behavioural therapy more effective than relaxation therapy in the treatment of anxiety disorders? A meta-analysis.* Psychological medicine, 2018. **48**(9): p. 1427-1436.

648. Mörtberg, E., et al., *Intensive cognitive-behavioral group treatment (CBGT) of social phobia: a randomized controlled study.* Journal of Anxiety Disorders, 2006. **20**(5): p. 646-660.

649. Murphy, M.T., et al., *The Role of Self-Directed In VivoExposure in Combination with Cognitive Therapy, Relaxation Training, or Therapist-Assisted Exposure in the Treatment of Panic Disorder with Agoraphobia.* Journal of Anxiety Disorders, 1998. **12**(2): p. 117-138.

650. Nadiga, D.N., P.L. Hensley, and E. Uhlenhuth, *Review of the long-term effectiveness of cognitive behavioral therapy compared to medications in panic disorder.* Depression and anxiety, 2003. **17**(2): p. 58-64.

651. Nations, K.R., et al., *Evaluation of the glycine transporter inhibitor Org 25935 as augmentation to cognitive-behavioral therapy for panic disorder: a multicenter, randomized, double-blind, placebo-controlled trial.* The Journal of clinical psychiatry, 2012. **73**(5): p. 647-653.

652. Newman, M.G., et al., *A randomized controlled trial of cognitive-behavioral therapy for generalized anxiety disorder with integrated techniques from emotion-focused and interpersonal therapies.* Journal of consulting and clinical psychology, 2011. **79**(2): p. 171.

653. Nordgreen, T., et al., *Stepped care versus direct face-to-face cognitive behavior therapy for social anxiety disorder and panic disorder: a randomized effectiveness trial.* Behavior Therapy, 2016. **47**(2): p. 166-183.

654. Öst, L.-G. and E. Breitholtz, *Applied relaxation vs. cognitive therapy in the treatment of generalized anxiety disorder.* Behaviour Research and Therapy, 2000. **38**(8): p. 777-790.

655. Otto, M.W., et al., *A comparison of the efficacy of clonazepam and cognitive-behavioral group therapy for the treatment of social phobia.* Journal of Anxiety Disorders, 2000. **14**(4): p. 345-358.

Copyright ©2021 Reed Group, Ltd.

656. Payne, L.A., et al., *SECOND-STAGE TREATMENTS FOR RELATIVE NONRESPONDERS TO COGNITIVE BEHAVIORAL THERAPY (CBT) FOR PANIC DISORDER WITH OR WITHOUT AGORAPHOBIA—CONTINUED CBT VERSUS SSRI: A RANDOMIZED CONTROLLED TRIAL.* Depression and anxiety, 2016. **33**(5): p. 392-399.

657. Ponniah, K. and S. Hollon, *Empirically supported psychological interventions for social phobia in adults: a qualitative review of randomized controlled trials.* Psychological medicine, 2008. **38**(1): p. 3-14.

658. Powell, V.B., et al., *Changing core beliefs with trial-based cognitive therapy may improve quality of life in social phobia: a randomized study.* Brazilian Journal of Psychiatry, 2013. **35**(3): p. 243-247.

659. Proudfoot, J., et al., *Clinical efficacy of computerised cognitive-behavioural therapy for anxiety and depression in primary care: randomised controlled trial.* The British Journal of Psychiatry, 2004. **185**(1): p. 46-54.

660. Roberge, P., et al., *Cognitive-behavioral treatment for panic disorder with agoraphobia: a randomized, controlled trial and cost-effectiveness analysis.* Behavior Modification, 2008. **32**(3): p. 333-351.

661. Roy-Byrne, P.P., et al., *A randomized effectiveness trial of cognitive-behavioral therapy and medication for primary care panic disorder.* Archives of General Psychiatry, 2005. **62**(3): p. 290-298.

662. Salzer, S., et al., *Long-term effects of short-term psychodynamic psychotherapy and cognitive-behavioural therapy in generalized anxiety disorder: 12-month follow-up.* The Canadian Journal of Psychiatry, 2011. **56**(8): p. 503-508.

663. Schreiber, F., et al., *Cognitive therapy for social anxiety disorder: The impact of the "self-focused attention and safety behaviours experiment" on the course of treatment.* Behavioural and cognitive psychotherapy, 2015. **43**(2): p. 158-166.

664. Schuurmans, J., et al., *A randomized, controlled trial of the effectiveness of cognitive–behavioral therapy and sertraline versus a waitlist control group for anxiety disorders in older adults.* The American journal of geriatric psychiatry, 2006. **14**(3): p. 255-263.

665. Schuurmans, J., et al., *Long-term effectiveness and prediction of treatment outcome in cognitive behavioral therapy and sertraline for late-life anxiety disorders.* International Psychogeriatrics, 2009. **21**(6): p. 1148-1159.

666. Schweden, T.L., et al., *Reduction of depersonalization during social stress through cognitive therapy for social anxiety disorder: A randomized controlled trial.* Journal of anxiety disorders, 2016. **43**: p. 99-105.

667. Sharp, D., K. Power, and V. Swanson, *A comparison of the efficacy and acceptability of group versus individual cognitive behaviour therapy in the treatment of panic disorder and agoraphobia in primary care.* Clinical Psychology & Psychotherapy: An International Journal of Theory & Practice, 2004. **11**(2): p. 73-82.

668. Smits, J.A., et al., *The efficacy of cognitive-behavioral interventions for reducing anxiety sensitivity: A meta-analytic review.* Behaviour research and therapy, 2008. **46**(9): p. 1047-1054.

669. Sørensen, P., et al., *A randomized clinical trial of cognitive behavioural therapy versus short-term psychodynamic psychotherapy versus no intervention for patients with hypochondriasis.* Psychological Medicine, 2011. **41**(2): p. 431-441.

670. Stangier, U., et al., *Cognitive therapy vs interpersonal psychotherapy in social anxiety disorder: a randomized controlled trial.* Archives of General Psychiatry, 2011. **68**(7): p. 692-700.

671. Stewart, R.E. and D.L. Chambless, *Cognitive–behavioral therapy for adult anxiety disorders in clinical practice: A meta-analysis of effectiveness studies.* Journal of consulting and clinical psychology, 2009. **77**(4): p. 595.

672. Telch, M.J., et al., *Group cognitive-behavioral treatment of panic disorder.* Behaviour research and therapy, 1993. **31**(3): p. 279-287.

673. Telch, M.J., et al., *Impact of cognitive-behavioral treatment on quality of life in panic disorder patients.* Journal of consulting and clinical psychology, 1995. **63**(5): p. 823.

Copyright ©2021 Reed Group, Ltd.

674. Thurston, M.D., et al., *Self-views in social anxiety disorder: The impact of CBT versus MBSR.* Journal of anxiety disorders, 2017. **47**: p. 83-90.

675. Thyer, B., *Cognitive behavioral group therapy and phenelzine both effective in social phobia.* Western journal of medicine, 1999. **171**(4): p. 240.

676. Tolin, D.F., *Is cognitive–behavioral therapy more effective than other therapies?: A meta-analytic review.* Clinical psychology review, 2010. **30**(6): p. 710-720.

677. Twomey, C., G. O'Reilly, and M. Byrne, *Effectiveness of cognitive behavioural therapy for anxiety and depression in primary care: a meta-analysis.* Family practice, 2014. **32**(1): p. 3-15.

678. Tyrer, H., et al., *Therapist differences in a randomised trial of the outcome of cognitive behaviour therapy for health anxiety in medical patients.* International journal of nursing studies, 2015. **52**(3): p. 686-694.

679. Vallury, K.D., M. Jones, and C. Oosterbroek, *Computerized cognitive behavior therapy for anxiety and depression in rural areas: a systematic review.* Journal of medical Internet research, 2015. **17**(6): p. e139.

680. Van Apeldoorn, F.J., et al., *Rate of improvement during and across three treatments for panic disorder with or without agoraphobia: cognitive behavioral therapy, selective serotonin reuptake inhibitor or both combined.* Journal of affective disorders, 2013. **150**(2): p. 313-319.

681. van Bronswijk, S.C., et al., *The influence of comorbid anxiety on the effectiveness of Cognitive Therapy and Interpersonal Psychotherapy for Major Depressive Disorder.* Journal of affective disorders, 2018. **232**: p. 52-60.

682. Watts, S.E., et al., *Treatment-as-usual (TAU) is anything but usual: a meta-analysis of CBT versus TAU for anxiety and depression.* Journal of affective disorders, 2015. **175**: p. 152-167.

683. Weck, F., et al., *Cognitive therapy versus exposure therapy for hypochondriasis (health anxiety): A randomized controlled trial.* Journal of Consulting and Clinical Psychology, 2015. **83**(4): p. 665.

684. Wells, A., et al., *A pilot randomized trial of metacognitive therapy vs applied relaxation in the treatment of adults with generalized anxiety disorder.* Behaviour research and therapy, 2010. **48**(5): p. 429-434.

685. White, K.S., et al., *Does maintenance CBT contribute to long-term treatment response of panic disorder with or without agoraphobia? A randomized controlled clinical trial.* Journal of Consulting and Clinical Psychology, 2013. **81**(1): p. 47.

686. Willutzki, U., T. Teismann, and D. Schulte, *Psychotherapy for social anxiety disorder: Long-term effectiveness of resource-oriented cognitive-behavioral therapy and cognitive therapy in social anxiety disorder.* Journal of Clinical Psychology, 2012. **68**(6): p. 581-591.

687. Zalta, A.K., *A meta-analysis of anxiety symptom prevention with cognitive-behavioral interventions.* Journal of anxiety disorders, 2011. **25**(5): p. 749-760.

688. Beutel, M.E., et al., *Implementing panic-focused psychodynamic psychotherapy into clinical practice.* The Canadian Journal of Psychiatry, 2013. **58**(6): p. 326-334.

689. Milrod, B., et al., *Psychotherapies for Panic Disorder: A Tale of Two Sites.* J Clin Psychiatry, 2016. **77**(7): p. 927-35.

690. Keefe, J.R., et al., *In-session emotional expression predicts symptomatic and panic-specific reflective functioning improvements in panic-focused psychodynamic psychotherapy.* Psychotherapy (Chic), 2019. **56**(4): p. 514-525.

691. Reinecke, A., et al., *Early effects of exposure-based cognitive behaviour therapy on the neural correlates of anxiety.* Translational psychiatry, 2018. **8**(1): p. 225.

692. Arch, J.J., et al., *Randomized clinical trial of cognitive behavioral therapy (CBT) versus acceptance and commitment therapy (ACT) for mixed anxiety disorders.* Journal of consulting and clinical psychology, 2012. **80**(5): p. 750.

Copyright ©2021 Reed Group, Ltd.

693. Pelissolo, A., et al., *Virtual reality exposure therapy versus cognitive behavior therapy for panic disorder with agoraphobia: a randomized comparison study.* Journal of Cybertherapy and Rehabilitation, 2012. **5**(1): p. 35-43.

694. Vos, S., et al., *A randomized clinical trial of cognitive behavioral therapy and interpersonal psychotherapy for panic disorder with agoraphobia.* Psychological Medicine, 2012. **42**(12): p. 2661-2672.

695. Robillard, G., et al., *Using virtual humans to alleviate social anxiety: preliminary report from a comparative outcome study.* Stud Health Technol Inform, 2010. **154**: p. 57-60.

696. Krijn, M., et al., *Fear of flying treatment methods: virtual reality exposure vs. cognitive behavioral therapy.* Aviation, space, and environmental medicine, 2007. **78**(2): p. 121-128.

697. Rezvan, S., et al., *A comparison of cognitive-behavior therapy with interpersonal and cognitive behavior therapy in the treatment of generalized anxiety disorder.* Counselling Psychology Quarterly, 2008. **21**(4): p. 309-321.

698. Bohn, C., et al., *Sudden gains in cognitive therapy and interpersonal therapy for social anxiety disorder.* Journal of consulting and clinical psychology, 2013. **81**(1): p. 177.

699. Lidren, D.M., et al., *A comparison of bibliotherapy and group therapy in the treatment of panic disorder.* Journal of consulting and clinical psychology, 1994. **62**(4): p. 865.

700. Febbraro, G.A., et al., *The limits of bibliotherapy: A study of the differential effectiveness of self-administered interventions in individuals with panic attacks.* Behavior Therapy, 1999. **30**(2): p. 209-222.

701. Wright, J., et al., *A bibliotherapy approach to relapse prevention in individuals with panic attacks.* Journal of Anxiety Disorders, 2000. **14**(5): p. 483-499.

702. Bower, P., D. Richards, and K. Lovell, *The clinical and cost-effectiveness of self-help treatments for anxiety and depressive disorders in primary care: a systematic review.* Br J Gen Pract, 2001. **51**(471): p. 838-845.

703. Jones, F.A., *The role of bibliotherapy in health anxiety: an experimental study.* British journal of community nursing, 2002. **7**(10): p. 498-504.

704. Febbraro, G.A., *An investigation into the effectiveness of bibliotherapy and minimal contact interventions in the treatment of panic attacks.* Journal of Clinical Psychology, 2005. **61**(6): p. 763-779.

705. Mead, N., et al., *The clinical effectiveness of guided self-help versus waiting-list control in the management of anxiety and depression: a randomized controlled trial.* Psychological Medicine, 2005. **35**(11): p. 1633-1643.

706. Andersson, G., et al., *Internet-based self-help with therapist feedback and in vivo group exposure for social phobia: a randomized controlled trial.* Journal of consulting and clinical psychology, 2006. **74**(4): p. 677.

707. Carlbring, P., et al., *An open study of Internet-based bibliotherapy with minimal therapist contact via email for social phobia.* Clinical Psychologist, 2006. **10**(1): p. 30-38.

708. Carlbring, P., et al., *Remote treatment of panic disorder: a randomized trial of internet-based cognitive behavior therapy supplemented with telephone calls.* American Journal of Psychiatry, 2006. **163**(12): p. 2119-2125.

709. Rapee, R.M., et al., *Treatment of social phobia through pure self-help and therapist-augmented self-help.* The British Journal of Psychiatry, 2007. **191**(3): p. 246-252.

710. Abramowitz, J.S., et al., *Self-help cognitive–behavioral therapy with minimal therapist contact for social phobia: a controlled trial.* Journal of Behavior Therapy and Experimental Psychiatry, 2009. **40**(1): p. 98-105.

711. Furmark, T., et al., *Guided and unguided self-help for social anxiety disorder: randomised controlled trial.* The British Journal of Psychiatry, 2009. **195**(5): p. 440-447.

Copyright ©2021 Reed Group, Ltd.

712. Nordin, S., et al., *Expanding the limits of bibliotherapy for panic disorder: randomized trial of self-help without support but with a clear deadline.* Behavior Therapy, 2010. **41**(3): p. 267-276.

713. Reeves, T., *A controlled study of assisted bibliotherapy.* Journal of Psychiatric & Mental Health Nursing, 2010. **17**(2): p. 184-190.

714. Carlbring, P., et al., *Individually-tailored, Internet-based treatment for anxiety disorders: A randomized controlled trial.* Behaviour Research and Therapy, 2011. **49**(1): p. 18-24.

715. Andersson, G., et al., *Internet-based psychodynamic versus cognitive behavioral guided self-help for generalized anxiety disorder: a randomized controlled trial.* Psychotherapy and psychosomatics, 2012. **81**(6): p. 344-355.

716. Haug, T., et al., *Self-help treatment of anxiety disorders: a meta-analysis and meta-regression of effects and potential moderators.* Clinical psychology review, 2012. **32**(5): p. 425-445.

717. Jeffcoat, T. and S.C. Hayes, *A randomized trial of ACT bibliotherapy on the mental health of K-12 teachers and staff.* Behaviour Research and Therapy, 2012. **50**(9): p. 571-579.

718. Taylor, B.L., et al., *The effectiveness of self-help mindfulness-based cognitive therapy in a student sample: a randomised controlled trial.* Behaviour Research and Therapy, 2014. **63**: p. 63-69.

719. Hedman, E., et al., *Exposure-based cognitive–behavioural therapy via the internet and as bibliotherapy for somatic symptom disorder and illness anxiety disorder: randomised controlled trial.* The British journal of psychiatry, 2016. **209**(5): p. 407-413.

720. Ritzert, T.R., et al., *Evaluating the effectiveness of ACT for anxiety disorders in a self-help context: Outcomes from a randomized wait-list controlled trial.* Behavior therapy, 2016. **47**(4): p. 444-459.

721. Hazlett-Stevens, H. and Y. Oren, *Effectiveness of Mindfulness-Based Stress Reduction Bibliotherapy: A Preliminary Randomized Controlled Trial.* Journal of clinical psychology, 2017. **73**(6): p. 626-637.

722. Twohig, M.P., et al., *Acceptance and commitment therapy as a treatment for anxiety disorders*, in *Acceptance and mindfulness-based approaches to anxiety*. 2005, Springer. p. 101-129.

723. Kocovski, N.L., J.E. Fleming, and N.A. Rector, *Mindfulness and acceptance-based group therapy for social anxiety disorder: An open trial.* Cognitive and Behavioral Practice, 2009. **16**(3): p. 276-289.

724. Arch, J.J., et al., *Longitudinal treatment mediation of traditional cognitive behavioral therapy and acceptance and commitment therapy for anxiety disorders.* Behaviour Research and Therapy, 2012. **50**(7-8): p. 469-478.

725. Wolitzky-Taylor, K.B., et al., *Moderators and non-specific predictors of treatment outcome for anxiety disorders: a comparison of cognitive behavioral therapy to acceptance and commitment therapy.* Journal of consulting and clinical psychology, 2012. **80**(5): p. 786.

726. Hayes-Skelton, S.A., L. Roemer, and S.M. Orsillo, *A randomized clinical trial comparing an acceptance-based behavior therapy to applied relaxation for generalized anxiety disorder.* Journal of consulting and clinical psychology, 2013. **81**(5): p. 761.

727. Swain, J., et al., *Acceptance and commitment therapy in the treatment of anxiety: a systematic review.* Clinical psychology review, 2013. **33**(8): p. 965-978.

728. Avdagic, E., S.A. Morrissey, and M.J. Boschen, *A randomised controlled trial of acceptance and commitment therapy and cognitive-behaviour therapy for generalised anxiety disorder.* Behaviour Change, 2014. **31**(2): p. 110-130.

729. Craske, M.G., et al., *Randomized controlled trial of cognitive behavioral therapy and acceptance and commitment therapy for social phobia: Outcomes and moderators.* Journal of consulting and clinical psychology, 2014. **82**(6): p. 1034.

Copyright ©2021 Reed Group, Ltd.

730. Gloster, A.T., et al., *Treating treatment-resistant patients with panic disorder and agoraphobia using psychotherapy: A randomized controlled switching trial.* Psychotherapy and psychosomatics, 2015. **84**(2): p. 100-109.

731. Kocovski, N.L., et al., *Mindfulness and acceptance-based group therapy and traditional cognitive behavioral group therapy for social anxiety disorder: Mechanisms of change.* Behaviour Research and Therapy, 2015. **70**: p. 11-22.

732. Millstein, D.J., et al., *Interpersonal problems, mindfulness, and therapy outcome in an acceptance-based behavior therapy for generalized anxiety disorder.* Cognitive behaviour therapy, 2015. **44**(6): p. 491-501.

733. Norton, A.R., et al., *A systematic review of mindfulness and acceptance-based treatments for social anxiety disorder.* Journal of clinical psychology, 2015. **71**(4): p. 283-301.

734. Eilenberg, T., et al., *Acceptance and commitment group therapy (ACT-G) for health anxiety: a randomized controlled trial.* Psychological medicine, 2016. **46**(1): p. 103-115.

735. Hacker, T., P. Stone, and A. MacBeth, *Acceptance and commitment therapy–do we know enough? Cumulative and sequential meta-analyses of randomized controlled trials.* Journal of affective disorders, 2016. **190**: p. 551-565.

736. Ivanova, E., et al., *Guided and unguided Acceptance and Commitment Therapy for social anxiety disorder and/or panic disorder provided via the Internet and a smartphone application: a randomized controlled trial.* Journal of anxiety disorders, 2016. **44**: p. 27-35.

737. Räsänen, P., et al., *An online guided ACT intervention for enhancing the psychological wellbeing of university students: A randomized controlled clinical trial.* Behaviour research and therapy, 2016. **78**: p. 30-42.

738. Eilenberg, T., et al., *Intervening variables in group-based acceptance & commitment therapy for severe health anxiety.* Behaviour research and therapy, 2017. **92**: p. 24-31.

739. Malmir, T., et al., *Determining the Effectiveness of Acceptance and Commitment Therapy (ACT) on Life Expectancy and Anxiety Among Bereaved Patients.* Materia socio-medica, 2017. **29**(4): p. 242.

740. Ducasse, D., et al., *Acceptance and commitment therapy for the management of suicidal patients: a randomized controlled trial.* Psychotherapy and psychosomatics, 2018. **87**(4): p. 211-222.

741. Grégoire, S., et al., *The use of acceptance and commitment therapy to promote mental health and school engagement in university students: A multisite randomized controlled trial.* Behavior therapy, 2018. **49**(3): p. 360-372.

742. Heydari, M., et al., *Effectiveness of Acceptance and Commitment Therapy on Anxiety and Depression of Razi Psychiatric Center Staff.* Open access Macedonian journal of medical sciences, 2018. **6**(2): p. 410.

743. Viskovich, S. and K.I. Pakenham, *Pilot evaluation of a web-based acceptance and commitment therapy program to promote mental health skills in university students.* Journal of clinical psychology, 2018. **74**(12): p. 2047-2069.

744. Kocovski, N.L., et al., *Self-help for social anxiety: Randomized controlled trial comparing a mindfulness and acceptance-based approach with a control group.* Behavior therapy, 2019. **50**(4): p. 696-709.

745. Macias, J., et al., *The efficacy of functional-analytic psychotherapy and acceptance and commitment therapy (FACT) for public employees.* Psicothema, 2019. **31**(1): p. 24-29.

746. Ritzert, T.R., et al., *Evaluating ACT Processes in Relation to Outcome in Self-Help Treatment for Anxiety-Related Problems.* Behavior Modification, 2019: p. 0145445519855616.

747. Markowitz, J.C., J. Lipsitz, and B.L. Milrod, *Critical review of outcome research on interpersonal psychotherapy for anxiety disorders.* Depression and anxiety, 2014. **31**(4): p. 316-325.

748. Hoffart, A., et al., *Change processes in residential cognitive and interpersonal psychotherapy for social phobia: A process-outcome study.* Behavior Therapy, 2009. **40**(1): p. 10-22.

Copyright ©2021 Reed Group, Ltd.

749. Dagöö, J., et al., *Cognitive behavior therapy versus interpersonal psychotherapy for social anxiety disorder delivered via smartphone and computer: a randomized controlled trial.* Journal of anxiety disorders, 2014. **28**(4): p. 410-417.

750. Lipsitz, J.D., et al., *A randomized trial of interpersonal therapy versus supportive therapy for social anxiety disorder.* Depression and anxiety, 2008. **25**(6): p. 542-553.

751. Borge, F.-M., et al., *Residential cognitive therapy versus residential interpersonal therapy for social phobia: A randomized clinical trial.* Journal of anxiety disorders, 2008. **22**(6): p. 991-1010.

752. Mewton, L., et al., *Current perspectives on Internet-delivered cognitive behavioral therapy for adults with anxiety and related disorders.* Psychology research and behavior management, 2014. **7**: p. 37.

753. Hedman, E., B. Ljótsson, and N. Lindefors, *Cognitive behavior therapy via the Internet: a systematic review of applications, clinical efficacy and cost–effectiveness.* Expert review of pharmacoeconomics & outcomes research, 2012. **12**(6): p. 745-764.

754. Waller, R. and S. Gilbody, *Barriers to the uptake of computerized cognitive behavioural therapy: a systematic review of the quantitative and qualitative evidence.* Psychological medicine, 2009. **39**(5): p. 705-712.

755. Cuijpers, P., et al., *Is guided self-help as effective as face-to-face psychotherapy for depression and anxiety disorders? A systematic review and meta-analysis of comparative outcome studies.* Psychological medicine, 2010. **40**(12): p. 1943-1957.

756. Arnberg, F.K., et al., *Internet-delivered psychological treatments for mood and anxiety disorders: a systematic review of their efficacy, safety, and cost-effectiveness.* PloS one, 2014. **9**(5): p. e98118.

757. Andrews, G., et al., *Computer therapy for the anxiety and depressive disorders is effective, acceptable and practical health care: a meta-analysis.* PloS one, 2010. **5**(10): p. e13196.

758. Bell, C.J., et al., *Effectiveness of computerised cognitive behaviour therapy for anxiety disorders in secondary care.* Australian & New Zealand Journal of Psychiatry, 2012. **46**(7): p. 630-640.

759. Titov, N., et al., *Randomized controlled trial of Internet cognitive behavioural treatment for social phobia with and without motivational enhancement strategies.* Australian & New Zealand Journal of Psychiatry, 2010. **44**(10): p. 938-945.

760. Titov, N., *Status of computerized cognitive behavioural therapy for adults.* Australian and New Zealand Journal of Psychiatry, 2007. **41**(2): p. 95-114.

761. Spek, V., et al., *Internet-based cognitive behaviour therapy for symptoms of depression and anxiety: a meta-analysis.* Psychological medicine, 2007. **37**(3): p. 319-328.

762. Peck, D., *Computer-guided cognitive–behavioural therapy for anxiety states.* Psychiatry, 2007. **6**(4): p. 166-169.

763. Andrews, G., et al., *Computer therapy for the anxiety and depression disorders is effective, acceptable and practical health care: an updated meta-analysis.* Journal of anxiety disorders, 2018. **55**: p. 70-78.

764. Kaltenthaler, E., G. Parry, and C. Beverley, *Computerized cognitive behaviour therapy: A systematic review.* Behavioural and Cognitive Psychotherapy, 2004. **32**(1): p. 31-55.

765. Dear, B.F., et al., *Clinical and cost-effectiveness of therapist-guided internet-delivered cognitive behavior therapy for older adults with symptoms of anxiety: a randomized controlled trial.* Behavior Therapy, 2015. **46**(2): p. 206-217.

766. Gingnell, M., et al., *Combining escitalopram and cognitive–behavioural therapy for social anxiety disorder: randomised controlled fMRI trial.* The British Journal of Psychiatry, 2016. **209**(3): p. 229-235.

Copyright ©2021 Reed Group, Ltd.

767. Hedman, E., et al., *Internet-based cognitive–behavioural therapy for severe health anxiety: randomised controlled trial.* The British Journal of Psychiatry, 2011. **198**(3): p. 230-236.

768. Hedman, E., et al., *Predictors of outcome in Internet-based cognitive behavior therapy for severe health anxiety.* Behaviour research and therapy, 2013. **51**(10): p. 711-717.

769. Carlbring, P., et al., *Treatment of social phobia: randomised trial of internet-delivered cognitive-behavioural therapy with telephone support.* The British Journal of Psychiatry, 2007. **190**(2): p. 123-128.

770. Titov, N., et al., *Transdiagnostic internet treatment for anxiety and depression: a randomised controlled trial.* Behaviour research and therapy, 2011. **49**(8): p. 441-452.

771. Newby, J.M., et al., *Internet cognitive behavioural therapy for mixed anxiety and depression: a randomized controlled trial and evidence of effectiveness in primary care.* Psychological Medicine, 2013. **43**(12): p. 2635-2648.

772. Andersson, G., et al., *Therapist experience and knowledge acquisition in internet-delivered CBT for social anxiety disorder: a randomized controlled trial.* PloS one, 2012. **7**(5): p. e37411.

773. Boettcher, J., et al., *Internet-based mindfulness treatment for anxiety disorders: a randomized controlled trial.* Behavior therapy, 2014. **45**(2): p. 241-253.

774. Nordgren, L.B., et al., *Effectiveness and cost-effectiveness of individually tailored Internet-delivered cognitive behavior therapy for anxiety disorders in a primary care population: a randomized controlled trial.* Behaviour research and therapy, 2014. **59**: p. 1-11.

775. Ruwaard, J., et al., *Web-based therapist-assisted cognitive behavioral treatment of panic symptoms: a randomized controlled trial with a three-year follow-up.* Journal of Anxiety Disorders, 2010. **24**(4): p. 387-396.

776. Wims, E., et al., *Clinician-assisted Internet-based treatment is effective for panic: A randomized controlled trial.* Australian and New Zealand Journal of Psychiatry, 2010. **44**(7): p. 599-607.

777. Berger, T., E. Hohl, and F. Caspar, *Internet-based treatment for social phobia: a randomized controlled trial.* Journal of clinical psychology, 2009. **65**(10): p. 1021-1035.

778. Ciuca, A.M., et al., *Internet-based treatment for panic disorder: A three-arm randomized controlled trial comparing guided (via real-time video sessions) with unguided self-help treatment and a waitlist control. PAXPD study results.* Journal of anxiety disorders, 2018. **56**: p. 43-55.

779. Berger, T., J. Boettcher, and F. Caspar, *Internet-based guided self-help for several anxiety disorders: A randomized controlled trial comparing a tailored with a standardized disorder-specific approach.* Psychotherapy, 2014. **51**(2): p. 207.

780. Boettcher, J., T. Berger, and B. Renneberg, *Does a pre-treatment diagnostic interview affect the outcome of Internet-based self-help for social anxiety disorder? A randomized controlled trial.* Behavioural and Cognitive Psychotherapy, 2012. **40**(5): p. 513-528.

781. Kenardy, J., K. McCafferty, and V. Rosa, *Internet-delivered indicated prevention for anxiety disorders: A randomized controlled trial.* Behavioural and Cognitive Psychotherapy, 2003. **31**(3): p. 279-289.

782. Oromendia, P., et al., *Internet-based self-help treatment for panic disorder: a randomized controlled trial comparing mandatory versus optional complementary psychological support.* Cognitive behaviour therapy, 2016. **45**(4): p. 270-286.

783. Paxling, B., et al., *Guided internet-delivered cognitive behavior therapy for generalized anxiety disorder: a randomized controlled trial.* Cognitive Behaviour Therapy, 2011. **40**(3): p. 159-173.

Copyright ©2021 Reed Group, Ltd.

784. Schröder, J., L. Jelinek, and S. Moritz, *A randomized controlled trial of a transdiagnostic Internet intervention for individuals with panic and phobias–One size fits all.* Journal of behavior therapy and experimental psychiatry, 2017. **54**: p. 17-24.

785. Proudfoot, J., et al., *Computerized, interactive, multimedia cognitive-behavioural program for anxiety and depression in general practice.* Psychological medicine, 2003. **33**(2): p. 217-227.

786. Andrews, G., M. Davies, and N. Titov, *Effectiveness randomized controlled trial of face to face versus Internet cognitive behaviour therapy for social phobia.* Australian & New Zealand Journal of Psychiatry, 2011. **45**(4): p. 337-340.

787. Craske, M.G., et al., *Computer-assisted delivery of cognitive behavioral therapy for anxiety disorders in primary-care settings.* Depression and anxiety, 2009. **26**(3): p. 235-242.

788. Dear, B., et al., *Transdiagnostic versus disorder-specific and clinician-guided versus self-guided internet-delivered treatment for Social Anxiety Disorder and comorbid disorders: a randomized controlled trial.* Journal of Anxiety Disorders, 2016. **42**: p. 30-44.

789. Lorian, C.N., N. Titov, and J.R. Grisham, *Changes in risk-taking over the course of an internet-delivered cognitive behavioral therapy treatment for generalized anxiety disorder.* Journal of anxiety disorders, 2012. **26**(1): p. 140-149.

790. Marks, I.M., et al., *Saving clinicians' time by delegating routine aspects of therapy to a computer: a randomized controlled trial in phobia/panic disorder.* Psychological Medicine, 2004. **34**(1): p. 9-17.

791. Neubauer, K., et al., *Internet-delivered attention modification training as a treatment for social phobia: A randomized controlled trial.* Behaviour research and therapy, 2013. **51**(2): p. 87-97.

792. Smith, K.L., et al., *Computer-delivered modeling of exposure for spider phobia: Relevant versus irrelevant exposure.* Journal of Anxiety Disorders, 1997. **11**(5): p. 489-497.

793. Carlbring, P., L. Ekselius, and G. Andersson, *Treatment of panic disorder via the Internet: a randomized trial of CBT vs. applied relaxation.* Journal of Behavior Therapy and Experimental Psychiatry, 2003. **34**(2): p. 129-140.

794. Carter, F.A., C.J. Bell, and H.C. Colhoun, *Suitability and acceptability of computerised cognitive behaviour therapy for anxiety disorders in secondary care.* Australian & New Zealand Journal of Psychiatry, 2013. **47**(2): p. 142-152.

795. Hedman, E., et al., *Internet-delivered exposure-based cognitive–behavioural therapy and behavioural stress management for severe health anxiety: randomised controlled trial.* The British Journal of Psychiatry, 2014. **205**(4): p. 307-314.

796. Hedman, E., et al., *The mediating effect of mindful non-reactivity in exposure-based cognitive behavior therapy for severe health anxiety.* Journal of anxiety disorders, 2017. **50**: p. 15-22.

797. Hedman-Lagerlöf, E., et al., *The impact of exposure-based cognitive behavior therapy for severe health anxiety on self-rated health: Results from a randomized trial.* Journal of psychosomatic research, 2017. **103**: p. 9-14.

798. Titov, N., G. Andrews, and P. Sachdev, *Computer-delivered cognitive behavioural therapy: effective and getting ready for dissemination.* F1000 medicine reports, 2010. **2**.

799. Johansson, R., et al., *Internet-based affect-focused psychodynamic therapy for social anxiety disorder: A randomized controlled trial with 2-year follow-up.* Psychotherapy (Chic), 2017. **54**(4): p. 351-360.

800. Bakker, A., et al., *Paroxetine, clomipramine, and cognitive therapy in the treatment of panic disorder.* The Journal of clinical psychiatry, 1999.

801. Marchand, A., et al., *Treatment of Panic Disorder with Agoraphobia: Randomized Placebo-Controlled Trial of Four Psychosocial Treatments Combined with Imipramine or Placebo.* Cognitive behaviour therapy, 2008. **37**(3): p. 146-159.

Copyright ©2021 Reed Group, Ltd.

802. Cottraux, J., et al., *A controlled study of cognitive behaviour therapy with buspirone or placebo in panic disorder with agoraphobia.* The British Journal of Psychiatry, 1995. **167**(5): p. 635-641.

803. Koszycki, D., et al., *A randomized trial of sertraline, self-administered cognitive behavior therapy, and their combination for panic disorder.* Psychol Med, 2011. **41**(2): p. 373-83.

804. Ritter, V., et al., *Changes in implicit and explicit self-esteem following cognitive and psychodynamic therapy in social anxiety disorder.* Psychotherapy Research, 2013. **23**(5): p. 547-558.

805. Strauß, B., et al., *Changes of attachment characteristics during psychotherapy of patients with social anxiety disorder: Results from the SOPHO-Net trial.* PLoS One, 2018. **13**(3): p. e0192802.

806. Oosterbaan, D.B., et al., *Cognitive therapy versus moclobemide in social phobia: a controlled study.* Clinical Psychology & Psychotherapy: An International Journal of Theory & Practice, 2001. **8**(4): p. 263-273.

807. Marcus, S.M., et al., *A comparison of medication side effect reports by panic disorder patients with and without concomitant cognitive behavior therapy.* American Journal of Psychiatry, 2007. **164**(2): p. 273-275.

808. Clark, D.M., et al., *A comparison of cognitive therapy, applied relaxation and imipramine in the treatment of panic disorder.* The British Journal of Psychiatry, 1994. **164**(6): p. 759-769.

809. Clark, D.M., et al., *Cognitive therapy versus fluoxetine in generalized social phobia: a randomized placebo-controlled trial.* Journal of consulting and clinical psychology, 2003. **71**(6): p. 1058.

810. Loerch, B., et al., *Randomised placebo-controlled trial of moclobemide, cognitive–behavioural therapy and their combination in panic disorder with agoraphobia.* The British Journal of Psychiatry, 1999. **174**(3): p. 205-212.

811. Zitrin, C.M., D.F. Klein, and M.G. Woerner, *Behavior therapy, supportive psychotherapy, imipramine, and phobias.* Archives of General Psychiatry, 1978. **35**(3): p. 307-316.

812. Bernik, M., et al., *Concomitant treatment with sertraline and social skills training improves social skills acquisition in social anxiety disorder: A double-blind, randomized controlled trial.* PloS one, 2018. **13**(10): p. e0205809.

813. Power, K., et al., *Controlled comparison of pharmacological and psychological treatment of generalized anxiety disorder in primary care.* Br J Gen Pract, 1990. **40**(336): p. 289-294.

814. Prasko, J., et al., *Moclobemide and cognitive behavioral therapy in the treatment of social phobia. A six-month controlled study and 24 months follow up.* Neuro Endocrinol Lett, 2006. **27**(4): p. 473-81.

815. van Apeldoorn, F.J., et al., *A randomized trial of cognitive-behavioral therapy or selective serotonin reuptake inhibitor or both combined for panic disorder with or without agoraphobia: treatment results through 1-year follow-up.* J Clin Psychiatry, 2010. **71**(5): p. 574-86.

816. Andersson, G., et al., *Therapeutic alliance in guided internet-delivered cognitive behavioural treatment of depression, generalized anxiety disorder and social anxiety disorder.* Behaviour research and therapy, 2012. **50**(9): p. 544-550.

817. Carlbring, P., et al., *All at once or one at a time? A randomized controlled trial comparing two ways to deliver bibliotherapy for panic disorder.* Cognitive behaviour therapy, 2011. **40**(3): p. 228-235.

818. Boersma, K., et al., *Efficacy of a transdiagnostic emotion-focused exposure treatment for chronic pain patients with comorbid anxiety and depression: a randomized controlled trial.* Pain, 2019. **160**(8): p. 1708-1718.

819. Neacsiu, A.D., et al., *Dialectical behavior therapy skills for transdiagnostic emotion dysregulation: a pilot randomized controlled trial.* Behav Res Ther, 2014. **59**: p. 40-51.

820. Neacsiu, A.D., et al., *Changes in Problematic Anger, Shame, and Disgust in Anxious and Depressed Adults Undergoing Treatment for Emotion Dysregulation.* Behavior Therapy, 2018. **49**: p. 344 -359.

Copyright ©2021 Reed Group, Ltd.

821. Staring, A.B., et al., *Self-esteem treatment in anxiety: A randomized controlled crossover trial of Eye Movement Desensitization and Reprocessing (EMDR) versus Competitive Memory Training (COMET) in patients with anxiety disorders.* Behav Res Ther, 2016. **82**: p. 11-20.

822. Abbass, A.A., *Intensive Short-Term Dynamic Psychotherapy of treatment-resistant depression: a pilot study.* Depression and Anxiety, 2006. **23**(7): p. 449-452.

823. Egger, N., et al., *Short-term cost-effectiveness of psychodynamic therapy and cognitive-behavioral therapy in social anxiety disorder: Results from the SOPHO-NET trial.* Journal of Affective Disorders, 2015. **180**: p. 21-28.

824. Heinonen, E., et al., *Therapists' professional and personal characteristics as predictors of outcome in short-and long-term psychotherapy.* Journal of Affective Disorders, 2012. **138**(3): p. 301-312.

825. Hunot, V., et al., *Psychological therapies for generalised anxiety disorder.* Cochrane Database of Systematic Reviews, 2007(1).

826. Knekt, P., et al., *Randomized trial on the effectiveness of long-and short-term psychotherapy on psychosocial functioning and quality of life during a 5-year follow-up.* Psychiatry Research, 2015. **229**(1-2): p. 381-388.

827. Knekt, P., et al., *Randomized trial on the effectiveness of long-and short-term psychodynamic psychotherapy and solution-focused therapy on psychiatric symptoms during a 3-year follow-up.* Psychological medicine, 2008. **38**(5): p. 689.

828. Laaksonen, M.A., P. Knekt, and O. Lindfors, *Psychological predictors of the recovery from mood or anxiety disorder in short-term and long-term psychotherapy during a 3-year follow-up.* Psychiatry Res, 2013. **208**(2): p. 162-73.

829. Mayo-Wilson, E., et al., *Psychological and pharmacological interventions for social anxiety disorder in adults: a systematic review and network meta-analysis.* Lancet Psychiatry, 2014. **1**(5): p. 368-76.

830. McCarthy, K.S., et al., *Twelve-month outcomes following successful panic-focused psychodynamic psychotherapy, cognitive-behavioral therapy, or applied relaxation training for panic disorder.* The Journal of clinical psychiatry, 2018. **79**(5): p. 0-0.

831. Milrod, B., et al., *A randomized controlled clinical trial of psychoanalytic psychotherapy for panic disorder.* Am J Psychiatry, 2007. **164**(2): p. 265-72.

832. Newman, M.G., et al., *Adult attachment as a moderator of treatment outcome for generalized anxiety disorder: Comparison between cognitive-behavioral therapy (CBT) plus supportive listening and CBT plus interpersonal and emotional processing therapy.* J Consult Clin Psychol, 2015. **83**(5): p. 915-925.

833. Wiltink, J., et al., *Transfer of manualized Short Term Psychodynamic Psychotherapy (STPP) for social anxiety disorder into clinical practice: results from a cluster-randomised controlled trial.* BMC psychiatry, 2017. **17**(1): p. 92.

834. Knijnik, D.Z., et al., *A pilot study of clonazepam versus psychodynamic group therapy plus clonazepam in the treatment of generalized social anxiety disorder.* Eur Psychiatry, 2008. **23**(8): p. 567-74.

835. Knijnik, D.Z., et al., *Defense style changes with the addition of psychodynamic group therapy to clonazepam in social anxiety disorder.* J Nerv Ment Dis, 2009. **197**(7): p. 547-51.

836. Flaxman, P.E. and F.W. Bond, *A randomised worksite comparison of acceptance and commitment therapy and stress inoculation training.* Behaviour research and therapy, 2010. **48**(8): p. 816-820.

837. Saunders, T., et al., *The effect of stress inoculation training on anxiety and performance.* Journal of occupational health psychology, 1996. **1**(2): p. 170.

838. Kirby, E.D., et al., *Psychosocial benefits of three formats of a standardized behavioral stress management program.* Psychosomatic medicine, 2006. **68**(6): p. 816-823.

Copyright ©2021 Reed Group, Ltd.

839. Lee, S.H., et al., *Effectiveness of a meditation-based stress management program as an adjunct to pharmacotherapy in patients with anxiety disorder.* Journal of Psychosomatic Research, 2007. **62**(2): p. 189-195.

840. Kitchiner, N.J., et al., *A randomized controlled trial comparing an adult education class using cognitive behavioural therapy ("stress control"), anxiety management group treatment and a waiting list for anxiety disorders.* Journal of Mental Health, 2009. **18**(4): p. 307-315.

841. Limm, H., et al., *Stress management interventions in the workplace improve stress reactivity: a randomised controlled trial.* Occupational and environmental medicine, 2011. **68**(2): p. 126-133.

842. Majid, S.A., et al., *Effect of mindfulness based stress management on reduction of generalized anxiety disorder.* Iranian journal of public health, 2012. **41**(10): p. 24.

843. Barrech, A., et al., *The long-term impact of a change in Effort–Reward imbalance on mental health—results from the prospective MAN-GO study.* The European Journal of Public Health, 2017. **27**(6): p. 1021-1026.

844. Corbett, C., J. Egan, and M. Pilch, *A randomised comparison of two 'Stress Control'programmes: Progressive Muscle Relaxation versus Mindfulness Body Scan.* Mental Health & Prevention, 2019. **15**: p. 200163.

845. Gould, C.E., et al., *Video-delivered relaxation intervention reduces late-life anxiety: a pilot randomized controlled trial.* The American Journal of Geriatric Psychiatry, 2019. **27**(5): p. 514-525.

846. Medisauskaite, A. and C. Kamau, *Reducing burnout and anxiety among doctors: Randomized controlled trial.* Psychiatry research, 2019.

847. Moskowitz, J.T., et al., *Randomized controlled trial of a facilitated online positive emotion regulation intervention for dementia caregivers.* Health Psychology, 2019. **38**(5): p. 391.

848. Niemeier, J.P., et al., *A Randomized Controlled Pilot Study of a Manualized Intervention for Caregivers of Patients With Traumatic Brain Injury in Inpatient Rehabilitation.* Archives of physical medicine and rehabilitation, 2019. **100**(4): p. S65-S75.

849. Stefanopoulou, E., et al., *Digitally Delivered Psychological Interventions for Anxiety Disorders: a Comprehensive Review.* Psychiatric Quarterly, 2019. **90**(1): p. 197-215.

850. Watanabe, N., et al., *Brief mindfulness-based stress management program for a better mental state in working populations-Happy Nurse Project: a randomized controlled trial.* Journal of Affective Disorders, 2019.

851. Shear, M.K., et al., *Emotion-focused psychotherapy for patients with panic disorder.* American Journal of Psychiatry, 2001. **158**(12): p. 1993-1998.

852. Balon, R., *Developments in treatment of anxiety disorders: psychotherapy, pharmacotherapy, and psychosurgery.* Depression and Anxiety, 2004. **19**(2): p. 63-76.

853. Schneider, A.J., et al., *Internet-guided self-help with or without exposure therapy for phobic and panic disorders.* Psychotherapy and psychosomatics, 2005. **74**(3): p. 154-164.

854. Guastella, A.J., et al., *A randomized controlled trial of D-cycloserine enhancement of exposure therapy for social anxiety disorder.* Biological psychiatry, 2008. **63**(6): p. 544-549.

855. Bögels, S.M., et al., *Psychodynamic psychotherapy versus cognitive behavior therapy for social anxiety disorder: an efficacy and partial effectiveness trial.* Depression and Anxiety, 2014. **31**(5): p. 363-373.

856. Hall, J., et al., *Efficacy of cognitive behavioral therapy for generalized anxiety disorder in older adults: systematic review, meta-analysis, and meta-regression.* The American Journal of Geriatric Psychiatry, 2016. **24**(11): p. 1063-1073.

Copyright ©2021 Reed Group, Ltd.

857. Imai, H., et al., *Psychological therapies versus pharmacological interventions for panic disorder with or without agoraphobia in adults.* Cochrane Database of Systematic Reviews, 2016(10).

858. Olthuis, J.V., et al., *Therapist-supported Internet cognitive behavioural therapy for anxiety disorders in adults.* Cochrane Database of Systematic Reviews, 2016(3).

859. Pompoli, A., et al., *Psychological therapies for panic disorder with or without agoraphobia in adults: a network meta-analysis.* Cochrane Database of Systematic Reviews, 2016(4).

860. Salt, S., C.A. Mulvaney, and N.J. Preston, *Drug therapy for symptoms associated with anxiety in adult palliative care patients.* Cochrane Database of Systematic Reviews, 2017(5).

861. Al-Yateem, N., et al., *Play distraction versus pharmacological treatment to reduce anxiety levels in children undergoing day surgery: a randomized controlled non-inferiority trial.* Child Care Health Dev, 2016. **42**(4): p. 572-81.

862. Brown, N.J., et al., *Efficacy of a children's procedural preparation and distraction device on healing in acute burn wound care procedures: study protocol for a randomized controlled trial.* Trials, 2012. **13**: p. 238.

863. Helbig-Lang, S., et al., *The strategy does not matter: Effects of acceptance, reappraisal, and distraction on the course of anticipatory anxiety in social anxiety disorder.* Psychol Psychother, 2015. **88**(4): p. 366-77.

864. Hudson, B.F., J. Ogden, and M.S. Whiteley, *Randomized controlled trial to compare the effect of simple distraction interventions on pain and anxiety experienced during conscious surgery.* Eur J Pain, 2015. **19**(10): p. 1447-55.

865. J.A., F., *Coping with the stress of a painful medical procedure.* Behaviour Research Therapy, 2002. **40**: p. 1003-1015.

866. Kim, H., et al., *Video Distraction and Parental Presence for the Management of Preoperative Anxiety and Postoperative Behavioral Disturbance in Children: A Randomized Controlled Trial.* Anesth Analg, 2015. **121**(3): p. 778-84.

867. Kwekkeboom, K., et al., *Randomized controlled trial of a brief cognitive-behavioral strategies intervention for the pain, fatigue, and sleep disturbance symptom cluster in advanced cancer.* Psychooncology, 2018. **27**(12): p. 2761-2769.

868. Lahmann, C., et al., *Brief relaxation versus music distraction in the treatment of dental anxiety: a randomized controlled clinical trial.* J Am Dent Assoc, 2008. **139**(3): p. 317-24.

869. Sogabe, M., et al., *The influence of various distractions prior to upper gastrointestinal endoscopy: a prospective randomized controlled study.* BMC Gastroenterol, 2018. **18**(1): p. 132.

870. Tanja-Dijkstra, K., *Can virtual nature improve patient experiences and memories of dental treatment? A study protocol for a randomized controlled trial.* BioMed Central, 2014. **15**(90).

871. Umezawa, S., et al., *Visual distraction alone for the improvement of colonoscopy-related pain and satisfaction.* World J Gastroenterol, 2015. **21**(15): p. 4707-14.

872. Walker, M.R., et al., *Treatment efficacy of virtual reality distraction in the reduction of pain and anxiety during cystoscopy.* Mil Med, 2014. **179**(8): p. 891-6.

873. Xiaolian, J., L. Xiaolin, and Z.H. Lan, *Effects of Visual and Audiovisual Distraction on Pain and Anxiety Among Patients Undergoing Colonoscopy.* Gastroenterology Nursing, 2015. **38**(1): p. 55-61.

874. Park, J.-M., et al., *Two-year follow-up after a randomised controlled trial of self-and clinician-accompanied exposure for phobia/panic disorders.* The British Journal of Psychiatry, 2001. **178**(6): p. 543-548.

875. Gega, L., I. Norman, and I. Marks, *Computer-aided vs. tutor-delivered teaching of exposure therapy for phobia/panic: randomized controlled trial with pre-registration nursing students.* International Journal of Nursing Studies, 2007. **44**(3): p. 397-405.

Copyright ©2021 Reed Group, Ltd.

876. Guastella, A.J., et al., *A randomized controlled trial of intranasal oxytocin as an adjunct to exposure therapy for social anxiety disorder.* Psychoneuroendocrinology, 2009. **34**(6): p. 917-923.

877. Kashdan, T.B., et al., *Can a one-hour session of exposure treatment modulate startle response and reduce spider fears?* Psychiatry research, 2012. **196**(1): p. 79-82.

878. Harned, M.S., et al., *Exposing clinicians to exposure: A randomized controlled dissemination trial of exposure therapy for anxiety disorders.* Behavior Therapy, 2014. **45**(6): p. 731-744.

879. Smits, J.A., et al., *Yohimbine enhancement of exposure therapy for social anxiety disorder: a randomized controlled trial.* Biological Psychiatry, 2014. **75**(11): p. 840-846.

880. Niles, A.N., et al., *Affect labeling enhances exposure effectiveness for public speaking anxiety.* Behaviour Research and Therapy, 2015. **68**: p. 27-36.

881. Hofmeijer-Sevink, M.K., et al., *No effects of D-cycloserine enhancement in exposure with response prevention therapy in panic disorder with agoraphobia: a double-blind, randomized controlled trial.* Journal of clinical psychopharmacology, 2017. **37**(5): p. 531-539.

882. Jayasinghe, N., et al., *Systematic review of the clinical application of exposure techniques to community-dwelling older adults with anxiety.* Clinical gerontologist, 2017. **40**(3): p. 141-158.

883. Meyerbroeker, K., et al., *Virtual reality exposure therapy does not provide any additional value in agoraphobic patients: a randomized controlled trial.* Psychotherapy and psychosomatics, 2013. **82**(3): p. 170-176.

884. Pyrkosch, L., et al., *Learn to forget: Does post-exposure administration of d-cycloserine enhance fear extinction in agoraphobia?* Journal of Psychiatric Research, 2018. **105**: p. 153-163.

885. Mumm, J.L.M., et al., *Heart rate variability in patients with agoraphobia with or without panic disorder remains stable during CBT but increases following in-vivo exposure.* Journal of anxiety disorders, 2019. **64**: p. 16-23.

886. Nunez, M., R.E. Zinbarg, and V.A. Mittal, *Efficacy and mechanisms of non-invasive brain stimulation to enhance exposure therapy: A review.* Clinical psychology review, 2019.

887. Raeder, F., et al., *Post-exposure cortisol administration does not augment the success of exposure therapy: A randomized placebo-controlled study.* Psychoneuroendocrinology, 2019. **99**: p. 174-182.

888. Sevinc, G., et al., *Strengthened Hippocampal Circuits Underlie Enhanced Retrieval of Extinguished Fear Memories Following Mindfulness Training.* Biological Psychiatry, 2019.

889. van Dis, E.A., et al., *Reducing negative stimulus valence does not attenuate the return of fear: Two counterconditioning experiments.* Behaviour Research and Therapy, 2019: p. 103416.

890. Rothbaum, B.O., et al., *A controlled study of virtual reality exposure therapy for the fear of flying.* Journal of consulting and clinical psychology, 2000. **68**(6): p. 1020.

891. Anderson, P.L., et al., *Virtual reality exposure therapy for social anxiety disorder: A randomized controlled trial.* Journal of consulting and clinical psychology, 2013. **81**(5): p. 751.

892. Ngai, I., E.C. Tully, and P.L. Anderson, *The course of the working alliance during virtual reality and exposure group therapy for social anxiety disorder.* Behavioural and cognitive psychotherapy, 2015. **43**(2): p. 167-181.

893. Kampmann, I.L., et al., *Exposure to virtual social interactions in the treatment of social anxiety disorder: A randomized controlled trial.* Behaviour research and therapy, 2016. **77**: p. 147-156.

894. Rothbaum, B.O., et al., *Virtual reality exposure therapy and standard (in vivo) exposure therapy in the treatment of fear of flying.* Behav Ther, 2006. **37**(1): p. 80-90.

Copyright ©2021 Reed Group, Ltd.

895. Meyerbröker, K., N. Morina, and P. Emmelkamp, *Enhancement of exposure therapy in participants with specific phobia: A randomized controlled trial comparing yohimbine, propranolol and placebo.* Journal of anxiety disorders, 2018. **57**: p. 48-56.

896. Marks, I.M., et al., *Alprazolam and exposure alone and combined in panic disorder with agoraphobia. A controlled study in London and Toronto.* Br J Psychiatry, 1993. **162**: p. 776-87.

897. Basoglu, M., et al., *Alprazolam and exposure for panic disorder with agoraphobia. Attribution of improvement to medication predicts subsequent relapse.* Br J Psychiatry, 1994. **164**(5): p. 652-9.

898. Acheson, D.T., et al., *Intranasal oxytocin administration prior to exposure therapy for arachnophobia impedes treatment response.* Depression and anxiety, 2015. **32**(6): p. 400-407.

899. Bouchard, S., et al., *Virtual reality compared with in vivo exposure in the treatment of social anxiety disorder: a three-arm randomised controlled trial.* The British Journal of Psychiatry, 2017. **210**(4): p. 276-283.

900. Tortella-Feliu, M., et al., *Virtual reality versus computer-aided exposure treatments for fear of flying.* Behavior modification, 2011. **35**(1): p. 3-30.

901. Botella, C., et al., *In vivo versus augmented reality exposure in the treatment of small animal phobia: a randomized controlled trial.* PloS one, 2016. **11**(2): p. e0148237.

902. Moldovan, R. and D. David, *ONE SESSION TREATMENT OF COGNITIVE AND BEHAVIORAL THERAPY AND VIRTUAL REALITY FOR SOCIAL AND SPECIFIC PHOBIAS. PRELIMINARY RESULTS FROM A RANDOMIZED CLINICAL TRIAL.* Journal of Evidence-Based Psychotherapies, 2014. **14**(1).

903. de Quervain, D.J., et al., *Glucocorticoids enhance extinction-based psychotherapy.* Proc Natl Acad Sci U S A, 2011. **108**(16): p. 6621-5.

904. Mühlberger, A., et al., *Repeated exposure of flight phobics to flights in virtual reality.* Behaviour research and therapy, 2001. **39**(9): p. 1033-1050.

905. Choi, Y.-H., et al., *Effects of group experiential cognitive therapy for the treatment of panic disorder with agoraphobia.* CyberPsychology & Behavior, 2005. **8**(4): p. 387-393.

906. Triscari, M.T., et al., *Effectiveness of cognitive behavioral therapy integrated with systematic desensitization, cognitive behavioral therapy combined with eye movement desensitization and reprocessing therapy, and cognitive behavioral therapy combined with virtual reality exposure therapy methods in the treatment of flight anxiety: a randomized trial.* Neuropsychiatric disease and treatment, 2015. **11**: p. 2591.

907. Pitti, C., et al., *The combined use of virtual reality exposure in the treatment of agoraphobia.* Actas espanolas de psiquiatria, 2015. **43**(4): p. 133.

908. Wallach, H.S., M.P. Safir, and M. Bar-Zvi, *Virtual Reality Exposure versus Cognitive Restructuring for Treatment of Public Speaking Anxiety: A Pilot Study.* The Israel Journal of Psychiatry and Related Sciences, 2011. **48**(2): p. 91.

909. Muhlberger, A., G. Wiedemann, and P. Pauli, *Efficacy of a one-session virtual reality exposure treatment for fear of flying.* Psychotherapy Research, 2003. **13**(3): p. 323-336.

910. Emmelkamp, P.M., et al., *Virtual reality treatment versus exposure in vivo: a comparative evaluation in acrophobia.* Behaviour research and therapy, 2002. **40**(5): p. 509-516.

911. North, M.M., S.M. North, and J.R. Coble, *Effectiveness of virtual environment desensitization in the treatment of agoraphobia.* Presence: Teleoperators & Virtual Environments, 1996. **5**(3): p. 346-352.

912. Castro, W.P., et al., *Cognitive-behavioral treatment and antidepressants combined with virtual reality exposure for patients with chronic agoraphobia.* International Journal of Clinical and Health Psychology, 2014. **14**(1): p. 9-17.

Copyright ©2021 Reed Group, Ltd.

913. Wallach, H.S., M.P. Safir, and M. Bar-Zvi, *Virtual reality cognitive behavior therapy for public speaking anxiety: a randomized clinical trial.* Behavior modification, 2009. **33**(3): p. 314-338.

914. Safir, M.P., H.S. Wallach, and M. Bar-Zvi, *Virtual reality cognitive-behavior therapy for public speaking anxiety: one-year follow-up.* Behavior modification, 2012. **36**(2): p. 235-246.

915. Wiederhold, B.K., et al., *The treatment of fear of flying: a controlled study of imaginal and virtual reality graded exposure therapy.* IEEE transactions on information technology in biomedicine, 2002. **6**(3): p. 218-223.

916. Gorini, A., et al., *Virtual reality in the treatment of generalized anxiety disorders.* Stud Health Technol Inform, 2010. **154**: p. 39-43.

917. Krijn, M., et al., *Treatment of acrophobia in virtual reality: The role of immersion and presence.* Behaviour research and therapy, 2004. **42**(2): p. 229-239.

918. Maltby, N., et al., *Virtual reality exposure therapy for the treatment of fear of flying: A controlled investigation.* Journal of consulting and clinical psychology, 2002. **70**(5): p. 1112.

919. Puryear, H.B., C.T. Cayce, and M.A. Thurston, *Anxiety reduction associated with meditation: home study.* Perceptual and motor skills, 1976. **43**(2): p. 527-531.

920. Peterson, L.G. and L. Pbert, *Effectiveness of a meditation-based stress reduction program in the treatment of anxiety disorders.* Am J Psychiatry, 1992. **149**(7): p. 936-43.

921. Evans, S., et al., *Mindfulness-based cognitive therapy for generalized anxiety disorder.* Journal of anxiety disorders, 2008. **22**(4): p. 716-721.

922. Manzoni, G.M., et al., *Relaxation training for anxiety: a ten-years systematic review with meta-analysis.* BMC psychiatry, 2008. **8**(1): p. 41.

923. Chen, K.W., et al., *Meditative therapies for reducing anxiety: A systematic review and meta-analysis of randomized controlled trials.* Depression and anxiety, 2012. **29**(7): p. 545-562.

924. Kocovski, N.L., et al., *Mindfulness and acceptance-based group therapy versus traditional cognitive behavioral group therapy for social anxiety disorder: A randomized controlled trial.* Behaviour Research and Therapy, 2013. **51**(12): p. 889-898.

925. Morgan, J.R., et al., *Cognitive processes as mediators of the relation between mindfulness and change in social anxiety symptoms following cognitive behavioral treatment.* Anxiety, Stress, & Coping, 2014. **27**(3): p. 288-302.

926. Orme-Johnson, D.W. and V.A. Barnes, *Effects of the transcendental meditation technique on trait anxiety: a meta-analysis of randomized controlled trials.* The Journal of Alternative and Complementary Medicine, 2014. **20**(5): p. 330-341.

927. Strauss, C., et al., *Mindfulness-based interventions for people diagnosed with a current episode of an anxiety or depressive disorder: a meta-analysis of randomised controlled trials.* PLOS one, 2014. **9**(4): p. e96110.

928. Smith, B., et al., *Short-form mindfulness-based stress reduction reduces anxiety and improves health-related quality of life in an inner-city population.* Holistic nursing practice, 2015. **29**(2): p. 70-77.

929. Hoge, E.A., et al., *Effects of mindfulness meditation on occupational functioning and health care utilization in individuals with anxiety.* Journal of psychosomatic research, 2017. **95**: p. 7-11.

930. Rodrigues, M.F., A.E. Nardi, and M. Levitan, *Mindfulness in mood and anxiety disorders: a review of the literature.* Trends in psychiatry and Psychotherapy, 2017. **39**(3): p. 207-215.

Copyright ©2021 Reed Group, Ltd.

931. Vøllestad, J., B. Sivertsen, and G.H. Nielsen, *Mindfulness-based stress reduction for patients with anxiety disorders: Evaluation in a randomized controlled trial.* Behaviour Research and Therapy, 2011. **49**(4): p. 281-288.

932. Basoglu, M., et al., *Pre-treatment predictors of treatment outcome in panic disorder and agoraphobia treated with alprazolam and exposure.* J Affect Disord, 1994. **30**(2): p. 123-32.

933. Wells, S., et al., *Evaluation of a meridian-based intervention, Emotional Freedom Techniques (EFT), for reducing specific phobias of small animals.* Journal of Clinical Psychology, 2003. **59**(9): p. 943-966.

934. Salas, M.M., A.J. Brooks, and J.E. Rowe, *The immediate effect of a brief energy psychology intervention (Emotional Freedom Techniques) on specific phobias: A pilot study.* Explore: The Journal of Science and Healing, 2011. **7**(3): p. 155-161.

935. Pignotti, M. and B. Thyer, *Some comments on "Energy psychology: A review of the evidence": Premature conclusions based on incomplete evidence?* Psychotherapy: Theory, Research, Practice, Training, 2009. **46**(2): p. 257-261.

936. Spielmans, G.I., G.M. Rosen, and T. Spence-Sing, *Tapping away at a misleading meta-analysis: No evidence for specificity of acupoint tapping.* Journal of Nervous and Mental Disease, 2020. **208**(8): p. 628-631.

937. Liebowitz, M.R., et al., *Phenelzine vs atenolol in social phobia. A placebo-controlled comparison.* Arch Gen Psychiatry, 1992. **49**(4): p. 290-300.

938. Merideth, C., et al., *Efficacy and tolerability of extended release quetiapine fumarate monotherapy in the acute treatment of generalized anxiety disorder: a randomized, placebo controlled and active-controlled study.* Int Clin Psychopharmacol, 2012. **27**(1): p. 40-54.

939. Bandelow, B., et al., *Extended-release quetiapine fumarate (quetiapine XR): a once-daily monotherapy effective in generalized anxiety disorder. Data from a randomized, double-blind, placebo- and active-controlled study.* Int J Neuropsychopharmacol, 2010. **13**(3): p. 305-20.

940. Baldwin, D.S., et al., *Efficacy of escitalopram in the treatment of social anxiety disorder: a meta-analysis versus placebo.* European Neuropsychopharmacology, 2016. **26**(6): p. 1062-1069.

941. Stocchi, F., et al., *Efficacy and tolerability of paroxetine for the long-term treatment of generalized anxiety disorder.* The Journal of clinical psychiatry, 2003. **64**(3): p. 250-258.

942. Wade, A., et al., *The effect of citalopram in panic disorder.* The British journal of psychiatry, 1997. **170**(6): p. 549-553.

943. Lepola, U.M., et al., *A controlled, prospective, 1-year trial of citalopram in the treatment of panic disorder.* The Journal of clinical psychiatry, 1998. **59**(10): p. 528-534.

944. Leinonen, E., et al., *Citalopram controls phobic symptoms in patients with panic disorder: randomized controlled trial.* Journal of Psychiatry and Neuroscience, 2000. **25**(1): p. 25.

945. Seedat, S., et al., *Reboxetine and citalopram in panic disorder: a single-blind, cross-over, flexible-dose pilot study.* International clinical psychopharmacology, 2003. **18**(5): p. 279-284.

946. Atmaca, M., et al., *Efficacy of citalopram and moclobemide in patients with social phobia: some preliminary findings.* Human Psychopharmacology: Clinical and Experimental, 2002. **17**(8): p. 401-405.

947. Lenze, E.J., et al., *Elevated cortisol in older adults with generalized anxiety disorder is reduced by treatment: a placebo-controlled evaluation of escitalopram.* The American Journal of Geriatric Psychiatry, 2011. **19**(5): p. 482-490.

948. Bose, A., et al., *Randomized placebo-controlled trial of escitalopram and venlafaxine XR in the treatment of generalized anxiety disorder.* Depression and anxiety, 2008. **25**(10): p. 854-861.

Copyright ©2021 Reed Group, Ltd.

949. Davidson, J.R., et al., *Escitalopram in the treatment of generalized anxiety disorder: Double-blind, placebo controlled, flexible-dose study.* Depression and anxiety, 2004. **19**(4): p. 234-240.

950. Bystritsky, A., et al., *A pilot controlled trial of bupropion XL versus escitalopram in generalized anxiety disorder.* Psychopharmacology bulletin, 2008. **41**(1): p. 46-51.

951. Allgulander, C., I. Florea, and A.K.T. Huusom, *Prevention of relapse in generalized anxiety disorder by escitalopram treatment.* International Journal of Neuropsychopharmacology, 2006. **9**(5): p. 495-505.

952. Asakura, S., et al., *A randomized, double-blind, placebo-controlled study of escitalopram in patients with social anxiety disorder in Japan.* Current medical research and opinion, 2016. **32**(4): p. 749-757.

953. Montgomery, S.A., et al., *A 24-week randomized, double-blind, placebo-controlled study of escitalopram for the prevention of generalized social anxiety disorder.* The Journal of clinical psychiatry, 2005. **66**(10): p. 1270-1278.

954. Kasper, S., et al., *Escitalopram in the treatment of social anxiety disorder: randomised, placebo-controlled, flexible-dosage study.* The British journal of psychiatry, 2005. **186**(3): p. 222-226.

955. Davidson, J., A. Bose, and Q. Wang, *Safety and efficacy of escitalopram in the long-term treatment of generalized anxiety disorder.* The Journal of clinical psychiatry, 2005. **66**(11): p. 1441-1446.

956. Stahl, S.M., I. Gergel, and D. Li, *Escitalopram in the treatment of panic disorder: a randomized, double-blind, placebo-controlled trial.* The Journal of clinical psychiatry, 2003. **64**(11): p. 1322-1327.

957. Lader, M., et al., *Efficacy and tolerability of escitalopram in 12-and 24-week treatment of social anxiety disorder: Randomised, double-blind, placebo-controlled, fixed-dose study.* Depression and anxiety, 2004. **19**(4): p. 241-248.

958. Stein, D.J., E.W. Andersen, and M. Lader, *Escitalopram versus paroxetine for social anxiety disorder: an analysis of efficacy for different symptom dimensions.* European neuropsychopharmacology, 2006. **16**(1): p. 33-38.

959. Baldwin, D.S., A.K.T. Huusom, and E. Mæhlum, *Escitalopram and paroxetine in the treatment of generalised anxiety disorder: randomised, placebo-controlled, double-blind study.* The British Journal of Psychiatry, 2006. **189**(3): p. 264-272.

960. Michelson, D., et al., *Efficacy of usual antidepressant dosing regimens of fluoxetine in panic disorder: randomised, placebo-controlled trial.* The British Journal of Psychiatry, 2001. **179**(6): p. 514-518.

961. Ribeiro, L., et al., *Mirtazapine versus fluoxetine in the treatment of panic disorder.* Brazilian Journal of Medical and Biological Research, 2001. **34**(10): p. 1303-1307.

962. Amore, M., et al., *Panic disorder. A long-term treatment study: fluoxetine vs imipramine.* Human Psychopharmacology: Clinical and Experimental, 1999. **14**(6): p. 429-434.

963. Michelson, D., et al., *Outcome assessment and clinical improvement in panic disorder: evidence from a randomized controlled trial of fluoxetine and placebo.* American Journal of Psychiatry, 1998. **155**(11): p. 1570-1577.

964. Tiller, J.W., C. Bouwer, and K. Behnke, *Moclobemide for anxiety disorders: a focus on moclobemide for panic disorder.* Int Clin Psychopharmacol, 1997. **12 Suppl 6**: p. S27-30.

965. Stein, D.J., et al., *Efficacy of paroxetine for relapse prevention in social anxiety disorder: a 24-week study.* Archives of General Psychiatry, 2002. **59**(12): p. 1111-1118.

966. Lepola, U., et al., *Controlled-release paroxetine in the treatment of patients with social anxiety disorder.* The Journal of clinical psychiatry, 2004. **65**(2): p. 222-229.

967. Allgulander, C., *Paroxetine in social anxiety disorder: a randomized placebo-controlled study.* Acta Psychiatrica Scandinavica, 1999. **100**(3): p. 193-198.

Copyright ©2021 Reed Group, Ltd.

968. Rickels, K., et al., *Paroxetine treatment of generalized anxiety disorder: a double-blind, placebo-controlled study.* American Journal of Psychiatry, 2003. **160**(4): p. 749-756.

969. Bielski, R.J., A. Bose, and C.-C. Chang, *A double-blind comparison of escitalopram and paroxetine in the long-term treatment of generalized anxiety disorder.* Annals of Clinical Psychiatry, 2005. **17**(2): p. 65-69.

970. Liebowitz, M.R., A.J. Gelenberg, and D. Munjack, *Venlafaxine extended release vs placebo and paroxetine in social anxiety disorder.* Archives of General Psychiatry, 2005. **62**(2): p. 190-198.

971. Seedat, S. and M.B. Stein, *Double-blind, placebo-controlled assessment of combined clonazepam with paroxetine compared with paroxetine monotherapy for generalized social anxiety disorder.* J Clin Psychiatry, 2004. **65**(2): p. 244-8.

972. Giménez, M., et al., *Functional effects of chronic paroxetine versus placebo on the fear, stress and anxiety brain circuit in Social Anxiety Disorder: initial validation of an imaging protocol for drug discovery.* European Neuropsychopharmacology, 2014. **24**(1): p. 105-116.

973. Kasper, S., et al., *Lavender oil preparation Silexan is effective in generalized anxiety disorder–a randomized, double-blind comparison to placebo and paroxetine.* International Journal of Neuropsychopharmacology, 2014. **17**(6): p. 859-869.

974. Schutters, S.I., et al., *Paroxetine augmentation in patients with generalised social anxiety disorder, non-responsive to mirtazapine or placebo.* Human Psychopharmacology: Clinical and Experimental, 2011. **26**(1): p. 72-76.

975. Stein, M.B., *Medication treatments for panic disorder and social phobia.* Depression and Anxiety, 1998. **7**(3): p. 134-138.

976. KIM, T.S., et al., *Comparison of venlafaxine extended release versus paroxetine for treatment of patients with generalized anxiety disorder.* Psychiatry and clinical neurosciences, 2006. **60**(3): p. 347-351.

977. Pollack, M., et al., *A randomized controlled trial of venlafaxine ER and paroxetine in the treatment of outpatients with panic disorder.* Psychopharmacology, 2007. **194**(2): p. 233-242.

978. Lecrubier, Y., et al., *A comparison of paroxetine, clomipramine and placebo in the treatment of panic disorder.* Acta Psychiatrica Scandinavica, 1997. **95**(2): p. 145-152.

979. Prosser, J.M., et al., *A comparison of low-dose risperidone to paroxetine in the treatment of panic attacks: a randomized, single-blind study.* BMC psychiatry, 2009. **9**(1): p. 25.

980. Perna, G., et al., *A Comparison of Citalopram and Paroxetine in the Treatment of Panic Disorder: A Randomized, Single-Blind Study.* Pharmacopsychiatry, 2001. **34**(03): p. 85-90.

981. Oehrberg, S., et al., *Paroxetine in the treatment of panic disorder a randomised, double-blind, placebo-controlled study.* The British Journal of Psychiatry, 1995. **167**(3): p. 374-379.

982. Nardi, A.E., et al., *Psychopharmacotherapy of panic disorder: 8-week randomized trial with clonazepam and paroxetine.* Braz J Med Biol Res, 2011. **44**(4): p. 366-73.

983. Nardi, A.E., et al., *A randomized, naturalistic, parallel-group study for the long-term treatment of panic disorder with clonazepam or paroxetine.* Journal of clinical psychopharmacology, 2012. **32**(1): p. 120-126.

984. Kampman, M., et al., *A randomized, double-blind, placebo-controlled study of the effects of adjunctive paroxetine in panic disorder patients unsuccessfully treated with cognitive-behavioral therapy alone.* The Journal of clinical psychiatry, 2002. **63**(9): p. 772-777.

985. Ballenger, J.C., et al., *Double-blind, fixed-dose, placebo-controlled study of paroxetine in the treatment of panic disorder.* American Journal of Psychiatry, 1998. **155**(1): p. 36-42.

Copyright ©2021 Reed Group, Ltd.

986. Buoli, M., et al., *Slow vs standard up-titration of paroxetine in the treatment of panic disorder: A prospective randomized trial.* Psychiatry and clinical neurosciences, 2010. **64**(6): p. 612-619.

987. Bertani, A., et al., *Comparison of the treatment with paroxetine and reboxetine in panic disorder: a randomized, single-blind study.* Pharmacopsychiatry, 2004. **37**(05): p. 206-210.

988. Marchesi, C., et al., *Effect of pharmacological treatment on temperament and character in panic disorder.* Psychiatry research, 2008. **158**(2): p. 147-154.

989. Brawman-Mintzer, O., et al., *Sertraline treatment for generalized anxiety disorder: a randomized, double-blind, placebo-controlled study.* J Clin Psychiatry, 2006. **67**(6): p. 874-81.

990. Ball, S.G., et al., *Selective serotonin reuptake inhibitor treatment for generalized anxiety disorder: a double-blind, prospective comparison between paroxetine and sertraline.* Journal of Clinical Psychiatry, 2005. **66**(1): p. 94-99.

991. Steiner, M., et al., *Gender differences in clinical presentation and response to sertraline treatment of generalized anxiety disorder.* Human Psychopharmacology: Clinical and Experimental, 2005. **20**(1): p. 3-13.

992. Cvjetkovic-Bosnjak, M., et al., *Pregabalin versus sertraline in generalized anxiety disorder. An open label study.* Eur Rev Med Pharmacol Sci, 2015. **19**(11): p. 2120-2124.

993. Pollack, M.H., et al., *A double-blind randomized controlled trial of augmentation and switch strategies for refractory social anxiety disorder.* American Journal of Psychiatry, 2014. **171**(1): p. 44-53.

994. Van Ameringen, M.A., et al., *Sertraline treatment of generalized social phobia: a 20-week, double-blind, placebo-controlled study.* American Journal of Psychiatry, 2001. **158**(2): p. 275-281.

995. Liebowitz, M.R., et al., *Efficacy of sertraline in severe generalized social anxiety disorder: results of a double-blind, placebo-controlled study.* J Clin Psychiatry, 2003. **64**(7): p. 785-92.

996. Katzelnick, D.J., et al., *Sertraline for social phobia: a double-blind, placebo-controlled crossover study.* The American journal of psychiatry, 1995.

997. Pollack, M.H., et al., *Sertraline in the treatment of panic disorder: a flexible-dose multicenter trial.* Archives of general psychiatry, 1998. **55**(11): p. 1010-1016.

998. Bandelow, B., et al., *Sertraline versus paroxetine in the treatment of panic disorder: an acute, double-blind noninferiority comparison.* The Journal of clinical psychiatry, 2004. **65**(3): p. 405.

999. Rapaport, M.H., et al., *Sertraline treatment of panic disorder: results of a long-term study.* Acta Psychiatrica Scandinavica, 2001. **104**(4): p. 289-298.

1000. Pohl, R.B., R.M. Wolkow, and C.M. Clary, *Sertraline in the treatment of panic disorder: a double-blind multicenter trial.* American Journal of Psychiatry, 1998. **155**(9): p. 1189-1195.

1001. Londborg, P.D., et al., *Sertraline in the treatment of panic disorder: a multi-site, double-blind, placebo-controlled, fixed-dose investigation.* The British Journal of Psychiatry, 1998. **173**(1): p. 54-60.

1002. Gommoll, C., et al., *A double-blind, randomized, placebo-controlled, fixed-dose phase III study of vilazodone in patients with generalized anxiety disorder.* Depression and anxiety, 2015. **32**(6): p. 451-459.

1003. Gommoll, C., et al., *Vilazodone in patients with generalized anxiety disorder: a double-blind, randomized, placebo-controlled, flexible-dose study.* International clinical psychopharmacology, 2015. **30**(6): p. 297.

1004. Durgam, S., et al., *Efficacy and Safety of Vilazodone in Patients With Generalized Anxiety Disorder: A Randomized, Double-Blind, Placebo-Controlled, Flexible-Dose Trial.* The Journal of clinical psychiatry, 2016. **77**(12): p. 1687-1694.

Copyright ©2021 Reed Group, Ltd.

1005. Careri, J.M., et al., *A 12-week double-blind, placebo-controlled, flexible-dose trial of vilazodone in generalized social anxiety disorder.* The primary care companion for CNS disorders, 2015. **17**(6).

1006. Simon, N.M., et al., *Duloxetine for the treatment of generalized social anxiety disorder: a preliminary randomized trial of increased dose to optimize response.* CNS spectrums, 2010. **15**(7): p. 436-443.

1007. Davidson, J., et al., *Efficacy and tolerability of duloxetine in elderly patients with generalized anxiety disorder: a pooled analysis of four randomized, double-blind, placebo-controlled studies.* Human Psychopharmacology: Clinical and Experimental, 2008. **23**(6): p. 519-526.

1008. Davidson, J.R., et al., *Efficacy, safety, and tolerability of venlafaxine extended release and buspirone in outpatients with generalized anxiety disorder.* J Clin Psychiatry, 1999. **60**(8): p. 528-35.

1009. Bodkin, J.A., et al., *Predictors of relapse in a study of duloxetine treatment for patients with generalized anxiety disorder.* Human Psychopharmacology: Clinical and Experimental, 2011. **26**(3): p. 258-266.

1010. Hartford, J., et al., *Duloxetine as an SNRI treatment for generalized anxiety disorder: results from a placebo and active-controlled trial.* International Clinical Psychopharmacology, 2007. **22**(3): p. 167-174.

1011. Mahableshwarkar, A., et al., *A randomised, double-blind, placebo-controlled, duloxetine-referenced study of the efficacy and tolerability of vortioxetine in the acute treatment of adults with generalised anxiety disorder.* International journal of clinical practice, 2014. **68**(1): p. 49-59.

1012. Rynn, M., et al., *Efficacy and safety of duloxetine in the treatment of generalized anxiety disorder: a flexible-dose, progressive-titration, placebo-controlled trial.* Depression and anxiety, 2008. **25**(3): p. 182-189.

1013. Alaka, K.J., et al., *Efficacy and safety of duloxetine in the treatment of older adult patients with generalized anxiety disorder: a randomized, double-blind, placebo-controlled trial.* International journal of geriatric psychiatry, 2014. **29**(9): p. 978-986.

1014. Koponen, H., et al., *Efficacy of duloxetine for the treatment of generalized anxiety disorder: implications for primary care physicians.* Primary care companion to the Journal of clinical psychiatry, 2007. **9**(2): p. 100.

1015. Montgomery, S.A., et al., *Efficacy and safety of pregabalin in the treatment of generalized anxiety disorder: a 6-week, multicenter, randomized, double-blind, placebo-controlled comparison of pregabalin and venlafaxine.* The Journal of clinical psychiatry, 2006. **67**(5): p. 771-782.

1016. Gelenberg, A.J., et al., *Efficacy of venlafaxine extended-release capsules in nondepressed outpatients with generalized anxiety disorder: a 6-month randomized controlled trial.* Jama, 2000. **283**(23): p. 3082-3088.

1017. Rickels, K., R. Mangano, and A. Khan, *A double-blind, placebo-controlled study of a flexible dose of venlafaxine ER in adult outpatients with generalized social anxiety disorder.* Journal of Clinical Psychopharmacology, 2004. **24**(5): p. 488-496.

1018. Bradwejn, J., et al., *Venlafaxine extended-release capsules in panic disorder: flexible-dose, double-blind, placebo-controlled study.* The British Journal of Psychiatry, 2005. **187**(4): p. 352-359.

1019. Allgulander, C., et al., *Efficacy of Venlafaxine ER in patients with social anxiety disorder: a double-blind, placebo-controlled, parallel-group comparison with paroxetine.* Human Psychopharmacology: Clinical and Experimental, 2004. **19**(6): p. 387-396.

1020. Noyes, R., Jr., et al., *Diazepam versus alprazolam for the treatment of panic disorder.* J Clin Psychiatry, 1996. **57**(8): p. 349-55.

1021. Krüger, M.B. and A.A. Dahl, *The efficacy and safety of moclobemide compared to clomipramine in the treatment of panic disorder.* European archives of psychiatry and clinical neuroscience, 1999. **249**(1): p. S19-S24.

Copyright ©2021 Reed Group, Ltd.

1022. Schneier, F.R., et al., *Placebo-controlled trial of moclobemide in social phobia.* British Journal of Psychiatry, 1998. **172**: p. 70-77.

1023. Versiani, M., et al., *Pharmacotherapy of social phobia. A controlled study with moclobemide and phenelzine.* Br J Psychiatry, 1992. **161**: p. 353-60.

1024. Tiller, J.W., C. Bouwer, and K. Behnke, *Moclobemide and fluoxetine for panic disorder. International Panic Disorder Study Group.* Eur Arch Psychiatry Clin Neurosci, 1999. **249 Suppl 1**: p. S7-10.

1025. Sheehan, D.V., J. Ballenger, and G. Jacobsen, *Treatment of endogenous anxiety with phobic, hysterical, and hypochondriacal symptoms.* Archives of General Psychiatry, 1980. **37**(1): p. 51-59.

1026. Nardi, A.E., et al., *Double-blind comparison of 30 and 60 mg tranylcypromine daily in patients with panic disorder comorbid with social anxiety disorder.* Psychiatry Res, 2010. **175**(3): p. 260-5.

1027. Wu, J., F. Chang, and H. Zu, *Efficacy and safety evaluation of citalopram and doxepin on sleep quality in comorbid insomnia and anxiety disorders.* Exp Ther Med, 2015. **10**(4): p. 1303-1308.

1028. Sheehan, D.V., et al., *Is buspirone effective for panic disorder?* J Clin Psychopharmacol, 1990. **10**(1): p. 3-11.

1029. Pohl, R., et al., *Serotonergic anxiolytics in the treatment of panic disorder: a controlled study with buspirone.* Psychopathology, 1989. **22 Suppl 1**: p. 60-7.

1030. Caillard, V., et al., *Comparative effects of low and high doses of clomipramine and placebo in panic disorder: a double-blind controlled study.* Acta Psychiatrica Scandinavica, 1999. **99**(1): p. 51-58.

1031. Fahy, T., et al., *The galway study of panic disorder I:: Clomipramine and lofepramine in DSM III-R panic disorder: A placebo controlled trial.* Journal of affective disorders, 1992. **25**(1): p. 63-75.

1032. Sasson, Y., et al., *A double-blind crossover comparison of clomipramine and desipramine in the treatment of panic disorder.* European Neuropsychopharmacology, 1999. **9**(3): p. 191-196.

1033. Modigh, K., P. Westberg, and E. Eriksson, *Superiority of clomipramine over imipramine in the treatment of panic disorder: a placebo-controlled trial.* Journal of Clinical Psychopharmacology, 1992.

1034. Johnston, D.G., I.E. Troyer, and S.F. Whitsett, *Clomipramine treatment of agoraphobic women: an eight-week controlled trial.* Archives of general psychiatry, 1988. **45**(5): p. 453-459.

1035. Gentil, V., et al., *Clomipramine, a better reference drug for panic/agoraphobia. I. Effectiveness comparison with imipramine.* Journal of Psychopharmacology, 1993. **7**(4): p. 316-324.

1036. Bianchi, G.N. and J. Phillips, *A comparative trial of doxepin and diazepam in anxiety states.* Psychopharmacologia, 1972. **25**(1): p. 86-95.

1037. Naftulin, D.H. and J.E. Ware, *A Behavioral and Clinical Evaluation of Two Psychotropic Agents: Doxepin - Hydrochloride & Perphenazine - Amitriptyline Hydrochloride.* Psychosomatics, 1972. **13**(2): p. 125-130.

1038. Goldberg, H.L. and R.J. Finnery, *The use of doxepin in the treatment of symptoms of anxiety neurosis and accompanying depression: a collaborative controlled study.* Am J Psychiatry, 1972. **129**(1): p. 74-7.

1039. Smith, M.E., *A controlled comparative study of doxepin and chlordiazepoxide in psychoneurotic anxiety.* J Clin Pharmacol New Drugs, 1971. **11**(2): p. 152-6.

1040. Khan, M.C., et al., *Mianserin and doxepin in the treatment of outpatient depression with anxiety.* Br J Clin Pharmacol, 1983. **15 Suppl 2**: p. 213s-218s.

Copyright ©2021 Reed Group, Ltd.

1041. Rosenberg, R., et al., *Alprazolam, imipramine and placebo treatment of panic disorder: predicting therapeutic response.* Acta Psychiatrica Scandinavica, 1991. **83**(365 S): p. 46-52.

1042. Nair, N., et al., *Comparison of fluvoxamine, imipramine, and placebo in the treatment of outpatients with panic disorder.* Anxiety, 1996. **2**(4): p. 192-198.

1043. Mavissakalian, M.R. and J.M. Perel, *Imipramine treatment of panic disorder with agoraphobia: dose ranging and plasma level-response relationships.* The American journal of psychiatry, 1995.

1044. Mavissakalian, M.R. and J.M. Perel, *Duration of imipramine therapy and relapse in panic disorder with agoraphobia.* Journal of Clinical Psychopharmacology, 2002. **22**(3): p. 294-299.

1045. Schweizer, E., et al., *Maintenance drug treatment of panic disorder: I. Results of a prospective, placebo-controlled comparison of alprazolam and imipramine.* Archives of General Psychiatry, 1993. **50**(1): p. 51-60.

1046. Zitrin, C.M., D.F. Klein, and M.G. Woerner, *Treatment of agoraphobia with group exposure in vivo and imipramine.* Archives of General Psychiatry, 1980. **37**(1): p. 63-72.

1047. Brodie, N., et al., *Anxiety/depression in elderly patients. A double-blind comparative study of fluphenazine/nortriptyline and promazine.* The Practitioner, 1975. **215**(1289): p. 660-664.

1048. Therapeutics, T.M.L.o.D.a., *Drugs for Depression.* The Medical Letter, 2016. **58**(1498): p. 85-90.

1049. Clinic, M. *Duloxetine (Oral Route)*. 2020; Available from: https://www.mayoclinic.org/drugs-supplements/duloxetine-oral-route/side-effects/drg-20067247?p=1.

1050. Therapeutics, T.M.L.o.D.a., *Drugs for Depression.* The Medical Letter, Inc., 2016. **58**(1498): p. 85-90.

1051. Therapeutics, T.M.L.o.D.a., *Nonopioid Drugs for Pain.* The Medical LEtter 2018. **60**(1540): p. 24-32.

1052. Therapeutics, T.M.L.o.D.a., *Drugs for Chronic Insomnia.* The Medical Letter, 2018. **60**(1562): p. 201-205.

1053. Therapeutics, T.M.L.o.D.a., *Drugs for Migraine.* The Medical Letter, 2017. **59**(1514): p. 27-32.

1054. WebMD. *Clomipramine HCL: Side Effects*. 2019; Available from: https://www.webmd.com/drugs/2/drug-1305/clomipramine-oral/details.

1055. Clinic, M. *Despiramine (Oral Route)*. 2020; Available from: https://www.mayoclinic.org/drugs-supplements/desipramine-oral-route/side-effects/drg-20071955.

1056. Clinic, M. *Doxepine (Oral Route)*. 2020; Available from: https://www.mayoclinic.org/drugs-supplements/doxepin-oral-route/side-effects/drg-20072083.

1057. Clinic, M. *Imipramine (Oral Route)*. 2020; Available from: https://www.mayoclinic.org/drugs-supplements/imipramine-oral-route/side-effects/drg-20072148.

1058. WebMD. *Phenelzine SULFATE: Side Effects*. 2019; Available from: https://www.webmd.com/drugs/2/drug-8827/phenelzine-oral/details.

1059. Clinic, M. *MAOIs and diet: Is it necessary to restrict tyramine?* 2018 Dec. 18, 2018; Available from: https://www.mayoclinic.org/diseases-conditions/depression/expert-answers/maois/faq-20058035.

1060. Clinic, M. *Monoamine oxidase inhibitors (MAOIs)*. 2019; Available from: https://www.mayoclinic.org/diseases-conditions/depression/in-depth/maois/art-20043992.

1061. Jakubovski, E., et al., *Systematic review and meta-analysis: dose-response relationship of selective serotonin reuptake inhibitors in major depressive disorder.* American Journal of Psychiatry, 2016. **173**(2): p. 174-183.

Copyright ©2021 Reed Group, Ltd.

1062. Rink, L., et al., *Dose increase versus unchanged continuation of antidepressants after initial antidepressant treatment failure in patients with major depressive disorder: a systematic review and meta-analysis of randomized, double-blind trials.* The Journal of clinical psychiatry, 2018. **79**(3): p. 0-0.

1063. Noyes Jr, R., et al., *Moclobemide in social phobia: a controlled dose-response trial.* Journal of clinical psychopharmacology, 1997. **17**(4): p. 247.

1064. Lenze, E.J., et al., *Escitalopram for older adults with generalized anxiety disorder: a randomized controlled trial.* Jama, 2009. **301**(3): p. 295-303.

1065. Figueira, M.L., *Alprazolam SR in the treatment of generalized anxiety: A multicentre controlled study with bromazepam.* Human Psychopharmacology, 1999. **14**(3): p. 171-177.

1066. Moller, H.J., et al., *Opipramol for the treatment of generalized anxiety disorder: a placebo-controlled trial including an alprazolam-treated group.* J Clin Psychopharmacol, 2001. **21**(1): p. 59-65.

1067. Hoehn-Saric, R., D.R. McLeod, and W.D. Zimmerli, *Differential effects of alprazolam and imipramine in generalized anxiety disorder: somatic versus psychic symptoms.* J Clin Psychiatry, 1988. **49**(8): p. 293-301.

1068. Stein, D.J., *Etifoxine versus alprazolam for the treatment of adjustment disorder with anxiety: a randomized controlled trial.* Adv Ther, 2015. **32**(1): p. 57-68.

1069. Elie, R. and Y. Lamontagne, *Alprazolam and diazepam in the treatment of generalized anxiety.* J Clin Psychopharmacol, 1984. **4**(3): p. 125-9.

1070. Aden, G.C. and S.G. Thein, Jr., *Alprazolam compared to diazepam and placebo in the treatment of anxiety.* J Clin Psychiatry, 1980. **41**(7): p. 245-8.

1071. Davison, K., et al., *A double-blind comparison of alprazolam, diazepam and placebo in the treatment of anxious out-patients.* British journal of clinical pharmacology, 1985. **19**(S1): p. 37S-43S.

1072. Enkelmann, R., *Alprazolam versus buspirone in the treatment of outpatients with generalized anxiety disorder.* Psychopharmacology (Berl), 1991. **105**(3): p. 428-32.

1073. Ballenger, J.C., et al., *Alprazolam in Panic Disorder and Agoraphobia: Results From a Multicenter Trial: I. Efficacy in Short-term Treatment.* Archives of General Psychiatry, 1988. **45**(5): p. 413-422.

1074. Ballenger, J., et al., *The first double-blind, placebo-controlled trial of a partial benzodiazepine agonist, abecarnil (ZK 112-119), in generalized anxiety disorder.* Advances in biochemical psychopharmacology, 1992. **47**: p. 431-447.

1075. Woodman, C.L., et al., *Predictors of response to alprazolam and placebo in patients with panic disorder.* J Affect Disord, 1994. **30**(1): p. 5-13.

1076. Curtis, G.C., et al., *Maintenance drug therapy of panic disorder.* J Psychiatr Res, 1993. **27 Suppl 1**: p. 127-42.

1077. Katschnig, H., et al., *Predictors of quality of life in a long-term followup study in panic disorder patients after a clinical drug trial.* Psychopharmacol Bull, 1996. **32**(1): p. 149-55.

1078. Andersch, S., L. Hanson, and T. Hällström, *Panic disorder: A Five-Year follow-up study in 52 patients.* European Journal of Psychiatry, 1997. **11**(3): p. 145-155.

1079. Andersch, S. and J. Hetta, *A 15-year follow-up study of patients with panic disorder.* Eur Psychiatry, 2003. **18**(8): p. 401-8.

1080. Andersch, S., et al., *Efficacy and safety of alprazolam, imipramine and placebo in treating panic disorder. A Scandinavian multicenter study.* Acta Psychiatrica Scandinavica, 1991. **83**(S365): p. 18-27.

Copyright ©2021 Reed Group, Ltd.

1081. Pecknold, J., et al., *A double-blind, placebo-controlled, multicenter study with alprazolam and extended-release alprazolam in the treatment of panic disorder.* J Clin Psychopharmacol, 1994. **14**(5): p. 314-21.

1082. Swinson, R.P., J.C. Pecknold, and K. Kuch, *Psychopharmacological treatment of panic disorder and related states: a placebo controlled study of alprazolam.* Prog Neuropsychopharmacol Biol Psychiatry, 1987. **11**(2-3): p. 105-13.

1083. Bond, A.J., et al., *Behavioural aggression in panic disorder after 8 weeks' treatment with alprazolam.* J Affect Disord, 1995. **35**(3): p. 117-23.

1084. Rizley, R., et al., *A comparison of alprazolam and imipramine in the treatment of agoraphobia and panic disorder.* Psychopharmacol Bull, 1986. **22**(1): p. 167-72.

1085. Holland, R.L., B.C. Musch, and I. Hindmarch, *Specific effects of benzodiazepines and tricyclic antidepressants in panic disorder: Comparisons of clomipramine with alprazolam SR and adinazolam SR.* Human Psychopharmacology, 1999. **14**(2): p. 119-124.

1086. Schweizer, E., *Once-a-day control of panic disorder: evidence from a placebo-controlled trial of alprazolam extended release.* Current Therapeutic Research, 1995. **56**(9): p. 966-968.

1087. Zitrin, C.M., et al., *Treatment of phobias: I. Comparison of imipramine hydrochloride and placebo.* Archives of general psychiatry, 1983. **40**(2): p. 125-138.

1088. Sarris, J., et al., *The acute effects of kava and oxazepam on anxiety, mood, neurocognition; and genetic correlates: a randomized, placebo-controlled, double-blind study.* Hum Psychopharmacol, 2012. **27**(3): p. 262-9.

1089. Vaisanen, E. and E. Jalkanen, *A double-blind study of alprazolam and oxazepam in the treatment of anxiety.* Acta Psychiatr Scand, 1987. **75**(5): p. 536-41.

1090. Akhondzadeh, S., et al., *Passionflower in the treatment of generalized anxiety: a pilot double-blind randomized controlled trial with oxazepam.* J Clin Pharm Ther, 2001. **26**(5): p. 363-7.

1091. Janecek, J., et al., *Oxazepam in the treatment of anxiety states: a controlled study.* J Psychiatr Res, 1966. **4**(3): p. 199-206.

1092. Fabre Jr. LF and D.M. McLendon, *Ketazolam administered once-a-day compared to clorazepate t.i.d. and placebo in a double blind study to anxious out-patients.* 1979. **25**: p. 710-720.

1093. Cohn, J.B., et al., *Double-blind comparison of buspirone and clorazepate in anxious outpatients.* The American Journal of Medicine, 1986. **80**(3, Supplement 2): p. 10-16.

1094. Magnus, R.V., B.C. Dean, and S.H. Curry, *Clorazepate: double blind crossover comparison of a single nightly dose with diazepam thrice daily in anxiety.* Diseases of the nervous system, 1977. **38**(10): p. 819-821.

1095. Itil, T.M., R.K. Shrivastava, and D.M. Collins, *A double-blind study comparing the efficacy and safety of a single bedtime dose of halazepam with clorazepate and placebo in anxious outpatients.* Current Therapeutic Research - Clinical and Experimental, 1983. **34**(3): p. 441-452.

1096. Ricca, J.J., *Clorazepate Dipotassium in Anxiety: A Clinical Trial with Diazepam and Placebo Controls.* The Journal of Clinical Pharmacology and New Drugs, 1972. **12**(7): p. 286-290.

1097. Burrows, G.D., et al., *A controlled comparative trial of clorazepate (Tranxene) and diazepam (Valium) for anxiety.* Med J Aust, 1977. **2**(16): p. 525-8.

1098. Henderson, J.G., *Value of a single night-time dose of potassium clorazepate in anxiety: A controlled trial comparison with diazepam.* Scottish Medical Journal, 1982. **27**(4): p. 292-296.

Copyright ©2021 Reed Group, Ltd.

1099. Harris, P.G., *Patient acceptance as a factor in the effectiveness of treatment: an open assessment of potassium clorazepate ('Tranxene') and lorazepam in anxiety.* Curr Med Res Opin, 1974. **2**(10): p. 664-8.

1100. Fresquet, A., et al., *Efficacy and safety of lesopitron in outpatients with generalized anxiety disorder.* Annals of Pharmacotherapy, 2000. **34**(2): p. 147-153.

1101. Ellison, R.J., Jr. and L.A. Cancellaro, *A study in the management of anxiety with lorazepam.* J Clin Pharmacol, 1978. **18**(4): p. 210-9.

1102. Fontaine, R., et al., *Bromazepam and lorazepam in generalized anxiety: a placebo-controlled study with measurement of drug plasma concentrations.* Acta Psychiatrica Scandinavica, 1986. **74**(5): p. 451-458.

1103. Laakmann, G., et al., *Buspirone and lorazepam in the treatment of generalized anxiety disorder in outpatients.* Psychopharmacology (Berl), 1998. **136**(4): p. 357-66.

1104. Cutler, N.R., et al., *A double-blind, placebo-controlled study comparing the efficacy and safety of ipsapirone versus lorazepam in patients with generalized anxiety disorder: a prospective multicenter trial.* J Clin Psychopharmacol, 1993. **13**(6): p. 429-37.

1105. Mandos, L.A., et al., *Placebo-controlled comparison of the clinical effects of rapid discontinuation of ipsapirone and lorazepam after 8 weeks of treatment for generalized anxiety disorder.* International Clinical Psychopharmacology, 1995. **10**(4): p. 251-256.

1106. de Jonghe, F., et al., *A Comparative Study of Suriclone, Lorazepam and Placebo in Anxiety Disorder.* Pharmacopsychiatry, 1989. **22**(06): p. 266-271.

1107. Herrera-Arellano, A., et al., *Therapeutic effectiveness of Galphimia glauca vs. lorazepam in generalized anxiety disorder. A controlled 15-week clinical trial.* Planta Med, 2012. **78**(14): p. 1529-35.

1108. Olgiati, S.G., *Clinical assessment of lorazepam in anxiety: a double-blind study.* Current therapeutic research, clinical and experimental, 1975. **17**(1): p. 13-22.

1109. McCurdy, L., *Lorazepam, a new benzodiazepine derivative, in the treatment of anxiety: a double-blind clinical evaluation.* American journal of psychiatry, 1979. **136**(2): p. 187-190.

1110. de Paula, A.F.M., *Intravenous lorazepam and diazepam in the treatment of acute anxiety states in the neurotic: A controlled study.* Clinical Therapeutics, 1977. **1**(2): p. 125-134.

1111. Diamond, B.I., et al., *A comparative study of alpidem, a nonbenzodiazepine, and lorazepam in patients with nonpsychotic anxiety.* Psychopharmacol Bull, 1991. **27**(1): p. 67-71.

1112. Charney, D.S. and S.W. Woods, *Benzodiazepine treatment of panic disorder: a comparison of alprazolam and lorazepam.* J Clin Psychiatry, 1989. **50**(11): p. 418-23.

1113. Lo, W.H. and T. Lo, *Clinical trial of benzoctamine versus chlordiazepoxide in anxiety neurosis.* J Clin Pharmacol New Drugs, 1973. **13**(1): p. 48-53.

1114. Lipman, R.S., et al., *Imipramine and chlordiazepoxide in depressive and anxiety disorders. I. Efficacy in depressed outpatients.* Arch Gen Psychiatry, 1986. **43**(1): p. 68-77.

1115. Rickels, K., et al., *Chlormezanone in anxiety: a drug rediscovered?* Am J Psychiatry, 1974. **131**(5): p. 592-5.

1116. Rickels, K., et al., *Long-term diazepam therapy and clinical outcome.* Jama, 1983. **250**(6): p. 767-771.

1117. Rickels, K., et al., *Antidepressants for the treatment of generalized anxiety disorder: a placebo-controlled comparison of imipramine, trazodone, and diazepam.* Archives of General Psychiatry, 1993. **50**(11): p. 884-895.

Copyright ©2021 Reed Group, Ltd.

1118. Rickels, K., et al., *Gepirone and diazepam in generalized anxiety disorder: a placebo-controlled trial.* Journal of clinical psychopharmacology, 1997. **17**(4): p. 272-277.

1119. Yamamoto, J., F.M. Kline, and R.W. Burgoyne, *The treatment of severe anxiety in outpatients: a controlled study comparing chlordiazepoxide and chlorpromazine.* Psychosomatics, 1973. **14**(1): p. 46-51.

1120. Davidson, J.R., et al., *Treatment of social phobia with clonazepam and placebo.* J Clin Psychopharmacol, 1993. **13**(6): p. 423-8.

1121. Goddard, A.W., et al., *Early coadministration of clonazepam with sertraline for panic disorder.* Arch Gen Psychiatry, 2001. **58**(7): p. 681-6.

1122. Nardi, A., et al., *Psychopharmacotherapy of panic disorder: 8-week randomized trial with clonazepam and paroxetine.* Brazilian Journal of Medical and Biological Research, 2011. **44**(4): p. 366-373.

1123. Jacobs, R.J., et al., *The effects of clonazepam on quality of life and work productivity in panic disorder.* Am J Manag Care, 1997. **3**(8): p. 1187-96.

1124. Pollack, M.H., et al., *Long-term outcome after acute treatment with alprazolam or clonazepam for panic disorder.* J Clin Psychopharmacol, 1993. **13**(4): p. 257-63.

1125. Hackett, D., V. Haudiquet, and E. Salinas, *A method for controlling for a high placebo response rate in a comparison of venlafaxine XR and diazepam in the short-term treatment of patients with generalised anxiety disorder.* European psychiatry, 2003. **18**(4): p. 182-187.

1126. Andreatini, R., et al., *Effect of valepotriates (valerian extract) in generalized anxiety disorder: a randomized placebo-controlled pilot study.* Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives, 2002. **16**(7): p. 650-654.

1127. Boyer, W. and J. Feighner, *A placebo-controlled double-blind multicenter trial of two doses of ipsapirone versus diazepam in generalized anxiety disorder.* International clinical psychopharmacology, 1993.

1128. Noyes, R., et al., *Diazepam and propranolol in panic disorder and agoraphobia.* Archives of General Psychiatry, 1984. **41**(3): p. 287-292.

1129. Fabre, L.F. and H.P. Putman, 3rd, *Depressive symptoms and intellectual functioning in anxiety patients treated with clorazepate.* J Clin Psychiatry, 1988. **49**(5): p. 189-92.

1130. Ramchandran, V., et al., *Comparative clinical evaluation of buspirone and diazepam in generalized anxiety disorders.* Current therapeutic research, 1990.

1131. Jacobson, A.F., et al., *Comparison of buspirone and diazepam in generalized anxiety disorder.* Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy, 1985. **5**(5): p. 290-296.

1132. OLAJIDE, D. and M. LADER, *A comparison of buspirone, diazepam, and placebo in patients with chronic anxiety states*. 1987, LWW.

1133. Petracca, A., et al., *Treatment of generalized anxiety disorder: Preliminary clinical experience with buspirone.* Journal of Clinical Psychiatry, 1990. **51**(9 SUPPL.): p. 31-39.

1134. Pecknold, J.C., et al., *Evaluation of buspirone as an antianxiety agent: buspirone and diazepam versus placebo.* The Canadian Journal of Psychiatry, 1989. **34**(8): p. 766-771.

1135. Pecknold, J.C., et al., *Alprazolam in panic disorder and agoraphobia: results from a multicenter trial. III. Discontinuation effects.* Arch Gen Psychiatry, 1988. **45**(5): p. 429-36.

Copyright ©2021 Reed Group, Ltd.

1136. Sheehan, D., et al., *The relative efficacy of high-dose buspirone and alprazolam in the treatment of panic disorder: a double-blind placebo-controlled study.* Acta Psychiatrica Scandinavica, 1993. **88**(1): p. 1-11.

1137. Wheatley, D., *Buspirone: multicenter efficacy study.* The Journal of clinical psychiatry, 1982.

1138. Islam, M.M., et al., *Benzodiazepine use and risk of dementia in the elderly population: a systematic review and meta-analysis.* Neuroepidemiology, 2016. **47**(3-4): p. 181-191.

1139. Noyes, R., Jr., et al., *Alprazolam in panic disorder and agoraphobia: results from a multicenter trial. II. Patient acceptance, side effects, and safety.* Arch Gen Psychiatry, 1988. **45**(5): p. 423-8.

1140. Davison, K., et al., *A double-blind comparison of alprazolam, diazepam and placebo in the treatment of anxious out-patients.* Br J Clin Pharmacol, 1985. **19 Suppl 1**: p. 37s-43s.

1141. Fabre, L.F., D.M. McLendon, and A. Mallette, *A double-blind comparison of prazepam with diazepam, chlorazepate dipotassium and placebo in anxious out-patients.* J Int Med Res, 1979. **7**(2): p. 147-51.

1142. Delle Chiaie, R., et al., *Assessment of the efficacy of buspirone in patients affected by generalized anxiety disorder, shifting to buspirone from prior treatment with lorazepam: a placebo-controlled, double-blind study.* J Clin Psychopharmacol, 1995. **15**(1): p. 12-9.

1143. Ravaris, C.L., et al., *A controlled study of alprazolam and propranolol in panic-disordered and agoraphobic outpatients.* Journal of clinical psychopharmacology, 1991.

1144. Munjack, D.J., et al., *Alprazolam, propranolol, and placebo in the treatment of panic disorder and agoraphobia with panic attacks.* Journal of clinical psychopharmacology, 1989.

1145. Meibach, R.C., et al., *Comparative efficacy of propranolol, chlordiazepoxide, and placebo in the treatment of anxiety: A double-blind trial.* The Journal of clinical psychiatry, 1987.

1146. Pande, A.C., et al., *Pregabalin in generalized anxiety disorder: a placebo-controlled trial.* American Journal of Psychiatry, 2003. **160**(3): p. 533-540.

1147. Feltner, D.E., et al., *A randomized, double-blind, placebo-controlled, fixed-dose, multicenter study of pregabalin in patients with generalized anxiety disorder.* Journal of clinical psychopharmacology, 2003. **23**(3): p. 240-249.

1148. Boerner, R., et al., *Kava-Kava extract LI 150 is as effective as Opipramol and Buspirone in Generalised Anxiety Disorder–an 8-week randomized, double-blind multi-centre clinical trial in 129 out-patients.* Phytomedicine, 2003. **10**: p. 38-49.

1149. Lader, M. and J.-C. Scotto, *A multicentre double-blind comparison of hydroxyzine, buspirone and placebo in patients with generalized anxiety disorder.* Psychopharmacology, 1998. **139**(4): p. 402-406.

1150. Sramek, J.J., E.J. Frackiewicz, and N.R. Cutlet, *Efficacy and safety of two dosing regimens of buspirone in the treatment of outpatients with persistent anxiety.* Clinical therapeutics, 1997. **19**(3): p. 498-506.

1151. Pecknold, J.C., et al., *Buspirone: anxiolytic?* Progress in Neuro-Psychopharmacology and Biological Psychiatry, 1985. **9**(5-6): p. 639-642.

1152. Böhm, C., et al., *A double-blind comparison of buspirone, clobazam, and placebo in patients with anxiety treated in a general practice setting.* J Clin Psychopharmacol, 1990. **10**(3 Suppl): p. 38s-42s.

1153. Fabre, L., *Double-blind comparison of buspirone with diazepam in anxious patients.* Current therapeutic research, 1987. **41**(5): p. 751-759.

1154. Scheibe, G., *Four-year follow-up in 40 out-patients with anxiety disorders buspirone versus lorazepam.* The European journal of psychiatry, 1996. **10**(1): p. 25-34.

Copyright ©2021 Reed Group, Ltd.

1155. Rickels, K., *Buspirone and diazepam in anxiety: a controlled study.* The Journal of clinical psychiatry, 1982.

1156. van Vliet, I.M., et al., *Clinical effects of buspirone in social phobia: a double-blind placebo-controlled study.* J Clin Psychiatry, 1997. **58**(4): p. 164-8.

1157. Sheehan, D.V., et al., *The relative efficacy of buspirone, imipramine and placebo in panic disorder: a preliminary report.* Pharmacol Biochem Behav, 1988. **29**(4): p. 815-7.

1158. Khan, A., et al., *A randomized, double-blind study of once-daily extended release quetiapine fumarate (quetiapine XR) monotherapy in patients with generalized anxiety disorder.* J Clin Psychopharmacol, 2011. **31**(4): p. 418-28.

1159. Khan, A., et al., *Extended-release quetiapine fumarate (quetiapine XR) as adjunctive therapy in patients with generalized anxiety disorder and a history of inadequate treatment response: a randomized, double-blind study.* Ann Clin Psychiatry, 2013. **25**(4): p. E7-22.

1160. Simon, N.M., et al., *Quetiapine augmentation of paroxetine CR for the treatment of refractory generalized anxiety disorder: preliminary findings.* Psychopharmacology (Berl), 2008. **197**(4): p. 675-81.

1161. Katzman, M.A., et al., *Extended release quetiapine fumarate (quetiapine XR) monotherapy as maintenance treatment for generalized anxiety disorder: a long-term, randomized, placebo-controlled trial.* Int Clin Psychopharmacol, 2011. **26**(1): p. 11-24.

1162. Altamura, A.C., et al., *Augmentative quetiapine in partial/nonresponders with generalized anxiety disorder: a randomized, placebo-controlled study.* Int Clin Psychopharmacol, 2011. **26**(4): p. 201-5.

1163. Goddard, A.W., et al., *A controlled trial of quetiapine XR coadministration treatment of SSRI-resistant panic disorder.* Annals of general psychiatry, 2015. **14**: p. 26-26.

1164. Diemer, J., et al., *Influence of single-dose quetiapine on fear network activity – A pharmaco-imaging study.* Progress in Neuro-Psychopharmacology and Biological Psychiatry, 2017. **76**: p. 80-87.

1165. Khan, A., et al., *Extended Release Quetiapine Fumarate (Quetiapine XR) as Adjunct Therapy in Patients with Generalized Anxiety Disorder and a History of Inadequate Treatment Response: A Randomized, Double-Blind Study.* Psychopharmacol Bull, 2011. **44**(2): p. 5-31.

1166. Kathol, R.G., et al., *Propranolol in chronic anxiety disorders: A controlled study.* Archives of General Psychiatry, 1980. **37**(12): p. 1361-1365.

1167. File, S.E. and R. Lister, *A comparison of the effects of lorazepam with those of propranolol on experimentally-induced anxiety and performance.* British journal of clinical pharmacology, 1985. **19**(4): p. 445-451.

1168. Becker, A., *Oxprenolol and propranolol in anxiety states. A double-blind comparative study.* South African medical journal= Suid-Afrikaanse tydskrif vir geneeskunde, 1976. **50**(16): p. 627-629.

1169. Munjack, D.J., et al., *Imipramine versus propranolol for the treatment of panic attacks: a pilot study.* Comprehensive psychiatry, 1985. **26**(1): p. 80-89.

1170. Peet, M. and S. Ali, *Propranolol and atenolol in the treatment of anxiety.* Int Clin Psychopharmacol, 1986. **1**(4): p. 314-9.

1171. Liebowitz, M.R., et al., *Pharmacotherapy of social phobia: an interim report of a placebo-controlled comparison of phenelzine and atenolol.* J Clin Psychiatry, 1988. **49**(7): p. 252-7.

1172. Wincor, M.Z., D.J. Munjack, and R. Palmer, *Alprazolam levels and response in panic disorder: preliminary results.* J Clin Psychopharmacol, 1991. **11**(1): p. 48-51.

Copyright ©2021 Reed Group, Ltd.

1173. Turner, S.M., D.C. Beidel, and R.G. Jacob, *Social phobia: a comparison of behavior therapy and atenolol.* J Consult Clin Psychol, 1994. **62**(2): p. 350-8.

1174. Clarke, H., et al., *Gabapentin reduces preoperative anxiety and pain catastrophizing in highly anxious patients prior to major surgery: a blinded randomized placebo-controlled trial.* Canadian Journal of Anesthesia/Journal canadien d'anesthésie, 2013. **60**(5): p. 432-443.

1175. Khezri, M.-B., M.-R. Oladi, and A. Atlasbaf, *Effect of melatonin and gabapentin on anxiety and pain associated with retrobulbar eye block for cataract surgery: a randomized double-blind study.* Indian journal of pharmacology, 2013. **45**(6): p. 581.

1176. Javaherforooshzadeh, F., et al., *Comparison of effects of melatonin and gabapentin on post operative anxiety and pain in lumbar spine surgery: A randomized clinical trial.* Anesthesiology and pain medicine, 2018. **8**(3).

1177. Tomaszek, L., et al., *Perioperative gabapentin in pediatric thoracic surgery patients—randomized, placebo-controlled, phase 4 trial.* Pain Medicine, 2020. **21**(8): p. 1562-1571.

1178. Lunn, T.H., et al., *Analgesic and sedative effects of perioperative gabapentin in total knee arthroplasty: a randomized, double-blind, placebo-controlled dose-finding study.* Pain, 2015. **156**(12): p. 2438-48.

1179. Pande, A.C., et al., *Placebo-controlled study of gabapentin treatment of panic disorder.* Journal of clinical psychopharmacology, 2000. **20**(4): p. 467-471.

1180. Tirault, M., et al., *Gabapentin premedication: Assessment of preoperative anxiolysis and postoperative patient satisfaction.* Acta Anaesthesiologica Belgica, 2010. **61**(4): p. 203-209.

1181. Kasper, S., et al., *Efficacy of pregabalin and venlafaxine-XR in generalized anxiety disorder: results of a double-blind, placebo-controlled 8-week trial.* Int Clin Psychopharmacol, 2009. **24**(2): p. 87-96.

1182. Kasper, S., et al., *Pregabalin long-term treatment and assessment of discontinuation in patients with generalized anxiety disorder.* The international journal of neuropsychopharmacology, 2014. **17**(5): p. 685-695.

1183. Rickels, K., et al., *Pregabalin for treatment of generalized anxiety disorder: a 4-week, multicenter, double-blind, placebo-controlled trial of pregabalin and alprazolam.* Archives of general psychiatry, 2005. **62**(9): p. 1022-1030.

1184. Greist, J.H., et al., *Efficacy of pregabalin in preventing relapse in patients with generalized social anxiety disorder: results of a double-blind, placebo-controlled 26-week study.* International clinical psychopharmacology, 2011. **26**(5): p. 243-251.

1185. Pohl, R.B., et al., *Efficacy of pregabalin in the treatment of generalized anxiety disorder: double-blind, placebo-controlled comparison of BID versus TID dosing.* Journal of clinical psychopharmacology, 2005. **25**(2): p. 151-158.

1186. Aliyev, N.A. and Z.N. Aliyev, *Valproate (depakine-chrono) in the acute treatment of outpatients with generalized anxiety disorder without psychiatric comorbidity: randomized, double-blind placebo-controlled study.* European Psychiatry, 2008. **23**(2): p. 109-114.

1187. Llorca, P.M., et al., *Efficacy and safety of hydroxyzine in the treatment of generalized anxiety disorder: a 3-month double-blind study.* J Clin Psychiatry, 2002. **63**(11): p. 1020-7.

1188. Darcis, T., et al., *A multicentre double-blind placebo-controlled study investigating the anxiolytic efficacy of hydroxyzine in patients with generalized anxiety.* Human Psychopharmacology: Clinical and Experimental, 1995. **10**(3): p. 181-187.

1189. Goldberg, H.L. and R.J. Finnerty, *The use of hydroxyzine (Vistaril) in the treatment of anxiety neurosis.* Psychosomatics, 1973. **14**(1): p. 38-41.

1190. Allgulander, C., et al., *Efficacy of sertraline in a 12-week trial for generalized anxiety disorder.* American Journal of Psychiatry, 2004. **161**(9): p. 1642-1649.

Copyright ©2021 Reed Group, Ltd.

1191. Mokhber, N., et al., *Randomized, single-blind, trial of sertraline and buspirone for treatment of elderly patients with generalized anxiety disorder.* Psychiatry and clinical neurosciences, 2010. **64**(2): p. 128-133.

1192. Davidson, J.R., et al., *Duloxetine treatment for relapse prevention in adults with generalized anxiety disorder: a double-blind placebo-controlled trial.* European Neuropsychopharmacology, 2008. **18**(9): p. 673-681.

1193. Nicolini, H., et al., *Improvement of psychic and somatic symptoms in adult patients with generalized anxiety disorder: examination from a duloxetine, venlafaxine extended-release and placebo-controlled trial.* Psychological medicine, 2009. **39**(2): p. 267-276.

1194. Bollu, V., et al., *Pregabalin reduces sleep disturbance in patients with generalized anxiety disorder via both direct and indirect mechanisms.* The European Journal of Psychiatry, 2010. **24**(1): p. 18-27.

1195. Stein, M.B., et al., *Efficacy of low and higher dose extended-release venlafaxine in generalized social anxiety disorder: a 6-month randomized controlled trial.* Psychopharmacology, 2005. **177**(3): p. 280-288.

1196. Klein, E., *Discontinuation of benzodiazepines in patients with anxiety disorders: a focus on alprazolam and alprazolam extended release.* Current Therapeutic Research, 1995. **56**(9): p. 969-974.

1197. Wallis, T.D., et al., *Single daily dose treatment of anxiety with clobazam or dipotassium clorazepate.* British journal of clinical pharmacology, 1979. **7 Suppl 1**: p. 123S-127S.

1198. Higueras, A., et al., *Bentazepam versus cloracepate in the treatment of anxiety disorders.* Current Therapeutic Research, 1992. **52**(1): p. 46-52.

1199. Bowden, C. and J. Fisher, *Safety and efficacy of long-term diazepam therapy.* Southern medical journal, 1980. **73**(12): p. 1581-1584.

1200. Boral GC, B.G., Oke VG, Jha RG, *Double-blind, randomized clinical evaluation of buspirone and diazepam in generalized anxiety disorders.*

1201. Feighner JP, M.C., Hendrickson GA, *A double-blind comparison of buspirone and diazepam in outpatients with generalized anxiety disorder.* J Clin Psychiatry, 1982. **43**: p. 103-108.

1202. Valarino, F. and R. Perez-Lopez, *Lorazepam and diazepam in the treatment of neurotic anxiety: a double-blind trial.* Dis Nerv Syst, 1976. **37**(2): p. 58-61.

1203. Cutler, N.R., et al., *The safety and efficacy of ipsapirone vs. lorazepam in outpatients with generalized anxiety disorder (GAD): single site findings from a multicenter trial.* Psychopharmacol Bull, 1993. **29**(2): p. 303-8.

1204. Woelk, H. and S. Schläfke, *A multi-center, double-blind, randomised study of the Lavender oil preparation Silexan in comparison to Lorazepam for generalized anxiety disorder.* Phytomedicine, 2010. **17**(2): p. 94-99.

1205. Herrera-Arellano, A., et al., *Efficacy and tolerability of a standardized herbal product from Galphimia glauca on generalized anxiety disorder. A randomized, double-blind clinical trial controlled with lorazepam.* Planta Medica, 2007. **73**(8): p. 713-717.

1206. Sheehan, D.V., et al., *Randomized, placebo-controlled trial of quetiapine XR and divalproex ER monotherapies in the treatment of the anxious bipolar patient.* Journal of affective disorders, 2013. **145**(1): p. 83-94.

1207. Stein, M.B., et al., *Paroxetine treatment of generalized social phobia (social anxiety disorder): a randomized controlled trial.* Jama, 1998. **280**(8): p. 708-713.

1208. Allgulander, C. and B. Nilsson, *A prospective study of 86 new patients with social anxiety disorder.* Acta Psychiatrica Scandinavica, 2001. **103**(6): p. 447-452.

Copyright ©2021 Reed Group, Ltd.

1209. Connor, K.M., et al., *Discontinuation of clonazepam in the treatment of social phobia.* Journal of clinical psychopharmacology, 1998. **18**(5): p. 373-378.

1210. Pollack, M.H., et al., *A double-blind study of the efficacy of venlafaxine extended-release, paroxetine, and placebo in the treatment of panic disorder.* Depression and anxiety, 2007. **24**(1): p. 1-14.

1211. Freire, R.C., et al., *A 6-year posttreatment follow-up of panic disorder patients: treatment with clonazepam predicts lower recurrence than treatment with paroxetine.* Journal of clinical psychopharmacology, 2017. **37**(4): p. 429-434.

1212. Pollack, M.H., et al., *Combined paroxetine and clonazepam treatment strategies compared to paroxetine monotherapy for panic disorder.* J Psychopharmacol, 2003. **17**(3): p. 276-82.

1213. Simon, N.M., et al., *Changes in anxiety sensitivity with pharmacotherapy for panic disorder.* J Psychiatr Res, 2004. **38**(5): p. 491-5.

1214. Klerman, G.L., *Drug Treatment of Panic Disorder: Comparative Efficacy of Alprazolam, Imipramine, and Placebo.* The British Journal of Psychiatry, 1992. **160**(2): p. 191-202.

1215. Dager, S.R., et al., *Long-term outcome of panic states during double-blind treatment and after withdrawal of alprazolam and placebo.* Annals of Clinical Psychiatry, 1992. **4**(4): p. 251-258.

1216. Schweizer, E., et al., *Lorazepam vs. alprazolam in the treatment of panic disorder.* Pharmacopsychiatry, 1990. **23**(2): p. 90-3.

1217. O'Sullivan, G.H., et al., *Alprazolam withdrawal symptoms in agoraphobia with panic disorder: Observations from a controlled Anglo-Canadian study.* Journal of Psychopharmacology, 1996. **10**(2): p. 101-109.

1218. Monteiro-dos-Santos, P., et al., *Effects of tryptophan depletion on anxiety induced by simulated public speaking.* Brazilian Journal of Medical and Biological Research, 2000. **33**(5): p. 581-587.

1219. Kim, J., et al., *Efficacy of α s1-casein hydrolysate on stress-related symptoms in women.* European journal of clinical nutrition, 2007. **61**(4): p. 536-541.

1220. Saeed, S.A., R.M. Bloch, and D.J. Antonacci, *Herbal and dietary supplements for treatment of anxiety disorders.* American family physician, 2007. **76**(4): p. 549-556.

1221. Jacka, F.N., et al., *Association between magnesium intake and depression and anxiety in community-dwelling adults: the Hordaland Health Study.* Australian and New Zealand Journal of Psychiatry, 2009. **43**(1): p. 45-52.

1222. Ulbricht, C., et al., *An evidence-based systematic review of rosemary (Rosmarinus officinalis) by the Natural Standard Research Collaboration.* Journal of dietary supplements, 2010. **7**(4): p. 351-413.

1223. Barbadoro, P., et al., *Fish oil supplementation reduces cortisol basal levels and perceived stress: A randomized, placebo-controlled trial in abstinent alcoholics.* Molecular nutrition & food research, 2013. **57**(6): p. 1110-1114.

1224. Boyle, N.B., C. Lawton, and L. Dye, *The effects of magnesium supplementation on subjective anxiety and stress—a systematic review.* Nutrients, 2017. **9**(5): p. 429.

1225. Colica, C., et al., *Evidences of a new psychobiotic formulation on body composition and anxiety.* Mediators of inflammation, 2017. **2017**.

1226. McCabe, D., et al., *The impact of essential fatty acid, B vitamins, vitamin C, magnesium and zinc supplementation on stress levels in women: a systematic review.* JBI database of systematic reviews and implementation reports, 2017. **15**(2): p. 402-453.

1227. Su, K.-P., et al., *Association of use of omega-3 polyunsaturated fatty acids with changes in severity of anxiety symptoms: A systematic review and meta-analysis.* JAMA network open, 2018. **1**(5): p. e182327-e182327.

Copyright ©2021 Reed Group, Ltd.

1228. Nishida, K., et al., *Health benefits of Lactobacillus gasseri CP2305 tablets in young adults exposed to chronic stress: A randomized, double-blind, placebo-controlled study.* Nutrients, 2019. **11**(8): p. 1859.

1229. Sarris, J., et al., *L-theanine in the adjunctive treatment of generalized anxiety disorder: A double-blind, randomised, placebo-controlled trial.* Journal of psychiatric research, 2019. **110**: p. 31-37.

1230. Tran, N., et al., *The gut-brain relationship: Investigating the effect of multispecies probiotics on anxiety in a randomized placebo-controlled trial of healthy young adults.* Journal of affective disorders, 2019. **252**: p. 271-277.

1231. Kobak, K.A., et al., *St. John's wort versus placebo in social phobia: results from a placebo-controlled pilot study.* Journal of Clinical Psychopharmacology, 2005. **25**(1): p. 51-58.

1232. Lehmann, E., E. Kinzler, and J. Friedemann, *Efficacy of a special kava extract (Piper methysticum) in patients with states of anxiety, tension and excitedness of non-mental origin—a double-blind placebo-controlled study of four weeks treatment.* Phytomedicine, 1996. **3**(2): p. 113-119.

1233. Volz, H.-P. and M. Kieser, *Kava-kava extract WS 1490 versus placebo in anxiety disorders-a randomized placebo-controlled 25-week outpatient trial.* Pharmacopsychiatry, 1997. **30**(01): p. 1-5.

1234. Pittler, M.H. and E. Ernst, *Efficacy of kava extract for treating anxiety: systematic review and meta-analysis.* Journal of clinical psychopharmacology, 2000. **20**(1): p. 84-89.

1235. Malsch, U. and M. Kieser, *Efficacy of kava-kava in the treatment of non-psychotic anxiety, following pretreatment with benzodiazepines.* Psychopharmacology, 2001. **157**(3): p. 277-283.

1236. Wheatley, D., *Kava-kava (LI 150) in the treatment of generalized anxiety disorder.* Primary Care Psychiatry, 2001. **7**(3): p. 97-100.

1237. Connor, K. and J. Davidson, *A placebo-controlled study of Kava kava in generalized anxiety disorder.* International clinical psychopharmacology, 2002. **17**(4): p. 185-188.

1238. Cagnacci, A., et al., *Kava–Kava administration reduces anxiety in perimenopausal women.* Maturitas, 2003. **44**(2): p. 103-109.

1239. Gastpar, M. and H. Klimm, *Treatment of anxiety, tension and restlessness states with Kava special extract WS® 1490 in general practice: A randomized placebo-controlled double-blind multicenter trial.* Phytomedicine, 2003. **10**(8): p. 631-639.

1240. Pittler, M.H. and E. Ernst, *Kava extract versus placebo for treating anxiety.* Cochrane database of systematic reviews, 2003(1).

1241. Geier, F. and T. Konstantinowicz, *Kava treatment in patients with anxiety.* Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives, 2004. **18**(4): p. 297-300.

1242. Jacobs, B.P., et al., *An internet-based randomized, placebo-controlled trial of kava and valerian for anxiety and insomnia.* Medicine, 2005. **84**(4): p. 197-207.

1243. Connor, K.M., V. Payne, and J.R. Davidson, *Kava in generalized anxiety disorder: three placebo-controlled trials.* International clinical psychopharmacology, 2006. **21**(5): p. 249-253.

1244. Ernst, E., *Herbal remedies for anxiety–a systematic review of controlled clinical trials.* Phytomedicine, 2006. **13**(3): p. 205-208.

1245. Sarris, J. and D.J. Kavanagh, *Kava and St. John's Wort: current evidence for use in mood and anxiety disorders.* The Journal of Alternative and Complementary Medicine, 2009. **15**(8): p. 827-836.

Copyright ©2021 Reed Group, Ltd.

1246. Sarris, J., et al., *The Kava Anxiety Depression Spectrum Study (KADSS): a randomized, placebo-controlled crossover trial using an aqueous extract of Piper methysticum.* Psychopharmacology, 2009. **205**(3): p. 399-407.

1247. Lakhan, S.E. and K.F. Vieira, *Nutritional and herbal supplements for anxiety and anxiety-related disorders: systematic review.* Nutrition journal, 2010. **9**(1): p. 42.

1248. Sarris, J., et al., *Kava in the treatment of generalized anxiety disorder: a double-blind, randomized, placebo-controlled study.* Journal of clinical psychopharmacology, 2013. **33**(5): p. 643-648.

1249. Zahreddine, N. and S. Richa, *Non-antidepressant treatment of generalized anxiety disorder.* Current clinical pharmacology, 2015. **10**(2): p. 86-96.

1250. Barić, H., et al., *Complementary and alternative medicine treatments for generalized anxiety disorder: systematic review and meta-analysis of randomized controlled trials.* Advances in therapy, 2018. **35**(3): p. 261-288.

1251. Ooi, S.L., P. Henderson, and S.C. Pak, *Kava for generalized anxiety disorder: A review of current evidence.* The Journal of Alternative and Complementary Medicine, 2018. **24**(8): p. 770-780.

1252. Savage, K., et al., *GABA-modulating phytomedicines for anxiety: A systematic review of preclinical and clinical evidence.* Phytotherapy research, 2018. **32**(1): p. 3-18.

1253. Smith, K. and C. Leiras, *The effectiveness and safety of Kava Kava for treating anxiety symptoms: A systematic review and analysis of randomized clinical trials.* Complementary therapies in clinical practice, 2018. **33**: p. 107-117.

1254. Sarris, J., et al., *Kava for generalised anxiety disorder: A 16-week double-blind, randomised, placebo-controlled study.* Australian & New Zealand Journal of Psychiatry, 2020. **54**(3): p. 288-297.

1255. Sarris, J., et al., *Kava for the treatment of generalized anxiety disorder RCT: analysis of adverse reactions, liver function, addiction, and sexual effects.* Phytotherapy Research, 2013. **27**(11): p. 1723-1728.

1256. Connor, K.M., et al., *Multidimensional effects of sertraline in social anxiety disorder.* Depression and anxiety, 2006. **23**(1): p. 6-10.

1257. Kasper, S., et al., *Silexan, an orally administered Lavandula oil preparation, is effective in the treatment of 'subsyndromal'anxiety disorder: a randomized, double-blind, placebo controlled trial.* International clinical psychopharmacology, 2010. **25**(5): p. 277-287.

1258. Kasper, S., I. Anghelescu, and A. Dienel, *Efficacy of orally administered Silexan in patients with anxiety-related restlessness and disturbed sleep–A randomized, placebo-controlled trial.* European neuropsychopharmacology, 2015. **25**(11): p. 1960-1967.

1259. Generoso, M.B., et al., *Lavender oil preparation (Silexan) for treating anxiety: an updated meta-analysis.* Journal of clinical psychopharmacology, 2017. **37**(1): p. 115-117.

1260. Kang, H.-J., et al., *How Strong is the Evidence for the Anxiolytic Efficacy of Lavender?: Systematic Review and Meta-analysis of Randomized Controlled Trials.* Asian nursing research, 2019.

1261. Kasper, S., et al., *Silexan in anxiety disorders: Clinical data and pharmacological background.* World J Biol Psychiatry, 2018. **19**(6): p. 412-420.

1262. Perry, R., et al., *Is lavender an anxiolytic drug? A systematic review of randomised clinical trials.* Phytomedicine, 2012. **19**(8-9): p. 825-35.

1263. Kasper, S., et al., *Silexan in generalized anxiety disorder: investigation of the therapeutic dosage range in a pooled data set.* International clinical psychopharmacology, 2017. **32**(4): p. 195-204.

Copyright ©2021 Reed Group, Ltd.

1264. Karaman, T., et al., *Evaluating the efficacy of lavender aromatherapy on peripheral venous cannulation pain and anxiety: A prospective, randomized study.* Complementary therapies in clinical practice, 2016. **23**: p. 64-68.

1265. Kasper, S., *An orally administered lavandula oil preparation (Silexan) for anxiety disorder and related conditions: an evidence based review.* International Journal of Psychiatry in Clinical Practice, 2013. **17**: p. 15-22.

1266. Chiappedi, M. and M. Bejor, *Herbals and natural dietary supplements in psychiatric practice.* Recent Patents on CNS Drug Discovery, 2010. **5**(2): p. 164-171.

1267. Hadley, S.K. and J.J. Petry, *Valerian.* American family physician, 2003. **67**(8): p. 1755-1758.

1268. Kinrys, G., E. Coleman, and E. Rothstein, *Natural remedies for anxiety disorders: potential use and clinical applications.* Depression and Anxiety, 2009. **26**(3): p. 259-265.

1269. Mischoulon, D., *The herbal anxiolytics kava and valerian for anxiety and insomnia.* Psychiatric Annals, 2002. **32**(1): p. 55-60.

1270. Roh, D., et al., *Valerian extract alters functional brain connectivity: A randomized double-blind placebo-controlled trial.* Phytotherapy Research, 2019. **33**(4): p. 939-948.

1271. Sundaresan, N., N. Kasthuri Bai, and I. Kaliappan, *VALERIANA OFFICINALIS: A REVIEW OF ITS TRADITIONAL USES, PHYTOCHEMISTRY AND PHARMACOLOGY.* Asian Journal of Pharmaceutical and Clinical Research, 2018. **11**(1).

1272. Bergamaschi, M.M., et al., *Cannabidiol reduces the anxiety induced by simulated public speaking in treatment-naive social phobia patients.* Neuropsychopharmacology, 2011. **36**(6): p. 1219-26.

1273. Black, N., et al., *Cannabinoids for the treatment of mental disorders and symptoms of mental disorders: a systematic review and meta-analysis.* Lancet Psychiatry, 2019. **6**(12): p. 995-1010.

1274. Blessing, E.M., et al., *Cannabidiol as a Potential Treatment for Anxiety Disorders.* Neurotherapeutics, 2015. **12**(4): p. 825-36.

1275. Crippa, J., A.W. Zuardi, and J. Hallak, *Therapeutical use of the cannabinoids in psychiatry.* Rev Bras Psiquiatr, 2010. **32**(Suppl 1): p. S56-S66.

1276. Crippa, J.A.S., et al., *Neural basis of anxiolytic effects of cannabidiol (CBD) in generalized social anxiety disorder: a preliminary report.* Journal of Psychopharmacology, 2011. **25**(1): p. 121-130.

1277. Danielsson, A.-K., et al., *Cannabis use, depression and anxiety: A 3-year prospective population-based study.* Journal of Affective Disorders, 2016. **193**: p. 103-108.

1278. Elms, L., et al., *Cannabidiol in the Treatment of Post-Traumatic Stress Disorder: A Case Series.* J Altern Complement Med, 2019. **25**(4): p. 392-397.

1279. Hoch, E., et al., *How effective and safe is medical cannabis as a treatment of mental disorders? A systematic review.* Eur Arch Psychiatry Clin Neurosci, 2019. **269**(1): p. 87-105.

1280. Khoury, J.M., et al., *Is there a role for cannabidiol in psychiatry?* World Journal of Biological Psychiatry, 2019. **20**(2): p. 101-116.

1281. Kosiba, J.D., S.A. Maisto, and J.W. Ditre, *Patient-reported use of medical cannabis for pain, anxiety, and depression symptoms: Systematic review and meta-analysis.* Social Science & Medicine, 2019. **233**: p. 181-192.

1282. Mandolini, G.M., et al., *Pharmacological properties of cannabidiol in the treatment of psychiatric disorders: a critical overview.* Epidemiology and psychiatric sciences, 2018. **27**(4): p. 327-335.

Copyright ©2021 Reed Group, Ltd.

1283. Moreira, F.A., M. Grieb, and B. Lutz, *Central side-effects of therapies based on CB1 cannabinoid receptor agonists and antagonists: focus on anxiety and depression.* Best Practice & Research Clinical Endocrinology & Metabolism, 2009. **23**(1): p. 133-144.

1284. Orsolini, L., et al., *Use of Medicinal Cannabis and Synthetic Cannabinoids in Post-Traumatic Stress Disorder (PTSD): A Systematic Review.* Medicina (Kaunas), 2019. **55**(9).

1285. Passie, T., et al., *Mitigation of post-traumatic stress symptoms by Cannabis resin: a review of the clinical and neurobiological evidence.* Drug Test Anal, 2012. **4**(7-8): p. 649-59.

1286. Rabinak, C.A. and K.L. Phan, *Cannabinoid modulation of fear extinction brain circuits: A novel target to advance anxiety treatment.* Current Pharmaceutical Design, 2014. **20**(13): p. 2212-2217.

1287. Steenkamp, M.M., et al., *Marijuana and other cannabinoids as a treatment for posttraumatic stress disorder: A literature review.* Depress Anxiety, 2017. **34**(3): p. 207-216.

1288. Tambaro, S. and M. Bortolato, *Cannabinoid-related agents in the treatment of anxiety disorders: current knowledge and future perspectives.* Recent Pat CNS Drug Discov, 2012. **7**(1): p. 25-40.

1289. Turna, J., B. Patterson, and M. Van Ameringen, *Is cannabis treatment for anxiety, mood, and related disorders ready for prime time?* Depression and anxiety, 2017. **34**(11): p. 1006-1017.

1290. Prasko, J., et al., *The effect of repetitive transcranial magnetic stimulation (rTMS) add on serotonin reuptake inhibitors in patients with panic disorder: a randomized, double blind sham controlled study.* Neuro Endocrinol Lett, 2007. **28**(1): p. 33-8.

1291. Li, H., et al., *Repetitive transcranial magnetic stimulation (rTMS) for panic disorder in adults.* Cochrane Database of Systematic Reviews, 2014(9).

1292. Diefenbach, G.J., et al., *Repetitive transcranial magnetic stimulation for generalised anxiety disorder: a pilot randomised, double-blind, sham-controlled trial.* The British Journal of Psychiatry, 2016. **209**(3): p. 222-228.

1293. Herrmann, M.J., et al., *Medial prefrontal cortex stimulation accelerates therapy response of exposure therapy in acrophobia.* Brain stimulation, 2017. **10**(2): p. 291-297.

1294. Huang, Z., et al., *Repetitive transcranial magnetic stimulation of the right parietal cortex for comorbid generalized anxiety disorder and insomnia: A randomized, double-blind, sham-controlled pilot study.* Brain stimulation, 2018. **11**(5): p. 1103-1109.

1295. Kumar, S., et al., *Effect of high-frequency repetitive transcranial magnetic stimulation (rTMS) in patients with comorbid panic disorder and major depression.* Australasian Psychiatry, 2018. **26**(4): p. 398-400.

1296. Cirillo, P., et al., *Transcranial magnetic stimulation in anxiety and trauma-related disorders: A systematic review and meta-analysis.* Brain and behavior, 2019. **9**(6): p. e01284.

1297. Griffiths, C., A. O'Neill-Kerr, and R.V. De, *Impact of repetitive transcranial magnetic stimulation on generalized anxiety disorder in treatment-resistant depression.* Annals of clinical psychiatry: official journal of the American Academy of Clinical Psychiatrists, 2019. **31**(3): p. e2-e7.

1298. Sagliano, L., et al., *Non-invasive brain stimulation in generalized anxiety disorder: A systematic review.* Progress in Neuro-Psychopharmacology and Biological Psychiatry, 2019.

1299. Vicario, C., et al., *A systematic review on the therapeutic effectiveness of non-invasive brain stimulation for the treatment of anxiety disorders.* Neuroscience & Biobehavioral Reviews, 2019. **96**: p. 219-231.

Copyright ©2021 Reed Group, Ltd.

1300. Dilkov D, H.E., Kaludiev E, Milev R., *Repetitive transcranial magnetic stimulation of the right dorsal lateral prefrontal cortex in the treatment of generalized anxiety disorder: A randomized, double-blind sham controlled clinical trial.* Prog Neuropsychopharmacol Biol Psychiatry, 2017. **78**: p. 61-65.

1301. Muller, W., et al., *Amelioration of psychiatric symptoms through exposure to music individually adapted to brain rhythm disorders - a randomised clinical trial on the basis of fundamental research.* Cogn Neuropsychiatry, 2014. **19**(5): p. 399-413.

1302. Morse, D.R. and E. Chow, *The effect of the Relaxodont brain wave synchronizer on endodontic anxiety: evaluation by galvanic skin resistance, pulse rate, physical reactions, and questionnaire responses.* Int J Psychosom, 1993. **40**(1-4): p. 68-76.

1303. Ossebaard, H.C., *Stress reduction by technology? An experimental study into the effects of brainmachines on burnout and state anxiety.* Appl Psychophysiol Biofeedback, 2000. **25**(2): p. 93-101.

1304. Ecsy, K., A.K.P. Jones, and C.A. Brown, *Alpha-range visual and auditory stimulation reduces the perception of pain.* European Journal of Pain, 2017. **21**(3): p. 562-572.

1305. Berg, K. and D. Siever, *A controlled comparison of audio-visual entrainment for treating seasonal affective disorder.* Journal of Neurotherapy, 2009. **13**(3): p. 166-175.

1306. Au, D.W., et al., *Effects of acupressure on anxiety: a systematic review and meta-analysis.* Acupunct Med, 2015. **33**(5): p. 353-9.

1307. Agarwal, A., et al., *Acupressure for prevention of pre-operative anxiety: a prospective, randomised, placebo controlled study.* Anaesthesia, 2005. **60**(10): p. 978-981.

1308. Bae, H., et al., *Efficacy of acupuncture in reducing preoperative anxiety: A meta-analysis.* Evidence-based Complementary and Alternative Medicine, 2014. **2014**.

1309. Kwon, C.Y. and B. Lee, *Acupuncture or Acupressure on Yintang (EX-HN 3) for Anxiety: A Preliminary Review.* Medical Acupuncture, 2018. **30**(2): p. 73-79.

1310. Monson, E., et al., *Beyond Pills: Acupressure Impact on Self-Rated Pain and Anxiety Scores.* J Altern Complement Med, 2019. **25**(5): p. 517-521.

1311. Tan, J.Y., et al., *Sham acupressure controls used in randomized controlled trials: A systematic review and critique.* PLoS ONE, 2015. **10**(7).

1312. Wang, S.-M. and Z.N. Kain, *Auricular acupuncture: a potential treatment for anxiety.* Anesthesia & Analgesia, 2001. **92**(2): p. 548-553.

1313. Wang, S.-M., C. Peloquin, and Z.N. Kain, *The use of auricular acupuncture to reduce preoperative anxiety.* Anesthesia & Analgesia, 2001. **93**(5): p. 1178-1180.

1314. Karst, M., et al., *Auricular acupuncture for dental anxiety: a randomized controlled trial.* Anesthesia & Analgesia, 2007. **104**(2): p. 295-300.

1315. Pilkington, K., et al., *Acupuncture for anxiety and anxiety disorders–a systematic literature review.* Acupuncture in Medicine, 2007. **25**(1-2): p. 1-10.

1316. Black, S., et al., *Determining the efficacy of auricular acupuncture for reducing anxiety in patients withdrawing from psychoactive drugs.* Journal of substance abuse treatment, 2011. **41**(3): p. 279-287.

1317. do Prado, J.M., L.F.S. Kurebayashi, and M.J.P. da Silva, *Auriculotherapy effectiveness in the reduction of anxiety in nursing students.* Revista da Escola de Enfermagem, 2012. **46**(5): p. 1200-1206.

Copyright ©2021 Reed Group, Ltd.

1318. Isoyama, D., et al., *Effect of acupuncture on symptoms of anxiety in women undergoing in vitro fertilisation: a prospective randomised controlled study.* Acupuncture in Medicine, 2012. **30**(2): p. 85-88.

1319. Michalek-Sauberer, A., et al., *Auricular acupuncture effectively reduces state anxiety before dental treatment—a randomised controlled trial.* Clinical oral investigations, 2012. **16**(6): p. 1517-1522.

1320. Chang, B.H. and E. Sommers, *Acupuncture and relaxation response for craving and anxiety reduction among military veterans in recovery from substance use disorder.* The American journal on addictions, 2014. **23**(2): p. 129-136.

1321. Errington-Evans, N., *Randomised controlled trial on the use of acupuncture in adults with chronic, non-responding anxiety symptoms.* Acupuncture in Medicine, 2015. **33**(2): p. 98-102.

1322. Ahlberg, R., et al., *Auricular acupuncture for substance use: a randomized controlled trial of effects on anxiety, sleep, drug use and use of addiction treatment services.* Substance abuse treatment, prevention, and policy, 2016. **11**(1): p. 24.

1323. de Lorent, L., et al., *Auricular acupuncture versus progressive muscle relaxation in patients with anxiety disorders or major depressive disorder: a prospective parallel group clinical trial.* Journal of acupuncture and meridian studies, 2016. **9**(4): p. 191-199.

1324. Klausenitz, C., et al., *Auricular Acupuncture for Exam Anxiety in Medical Students—A Randomized Crossover Investigation.* PloS one, 2016. **11**(12).

1325. Wiles, M., et al., *A randomised controlled trial examining the effect of acupuncture at the EX-HN 3 (Yintang) point on pre-operative anxiety levels in neurosurgical patients.* Anaesthesia, 2017. **72**(3): p. 335-342.

1326. Allan, F.K., et al., *Acupuncture for anxiety in dental patients: Systematic review and meta-analysis.* European Journal of Integrative Medicine, 2018. **20**: p. 22-35.

1327. Amorim, D., et al., *Acupuncture and electroacupuncture for anxiety disorders: A systematic review of the clinical research.* Complementary therapies in clinical practice, 2018. **31**: p. 31-37.

1328. Fleckenstein, J., P. Krüger, and K.-P. Ittner, *Effects of single-point acupuncture (HT7) in the prevention of test anxiety: Results of a RCT.* PloS one, 2018. **13**(8).

1329. Vieira, A., et al., *Clinical effect of auricular acupuncture in anxiety levels of students prior to the exams: A randomized controlled trial.* European Journal of Integrative Medicine, 2018. **20**: p. 188-192.

1330. Zeng, L., et al., *Electro-acupuncture improves psychiatric symptoms, anxiety and depression in methamphetamine addicts during abstinence: A randomized controlled trial.* Medicine, 2018. **97**(34).

1331. Dellovo, A., et al., *Effects of auriculotherapy and midazolam for anxiety control in patients submitted to third molar extraction.* International journal of oral and maxillofacial surgery, 2019. **48**(5): p. 669-674.

1332. Mak, A.D.P., et al., *Noneffectiveness of electroacupuncture for comorbid generalized anxiety disorder and irritable bowel syndrome.* Journal of gastroenterology and hepatology, 2019. **34**(10): p. 1736-1742.

1333. Amorim, D., et al., *Integrative medicine in anxiety disorders.* Complement Ther Clin Pract, 2018. **31**: p. 215-219.

1334. Edge, J., *A pilot study addressing the effect of aromatherapy massage on mood, anxiety and relaxation in adult mental health.* Complement Ther Nurs Midwifery, 2003. **9**(2): p. 90-7.

1335. Field, T.M., *Massage therapy effects.* Am Psychol, 1998. **53**(12): p. 1270-81.

1336. Kurebayashi, L.F.S., et al., *Massage and reiki used to reduce stress and anxiety: Randomized clinical trial.* Revista Latino-Americana de Enfermagem, 2016. **24**.

Copyright ©2021 Reed Group, Ltd.

1337. Moyer, C.A., J. Rounds, and J.W. Hannum, *A meta-analysis of massage therapy research.* Psychological bulletin, 2004. **130**(1): p. 3.

1338. Rapaport, M.H., et al., *Acute Swedish Massage Monotherapy Successfully Remediates Symptoms of Generalized Anxiety Disorder: A Proof-of-Concept, Randomized Controlled Study.* J Clin Psychiatry, 2016. **77**(7): p. e883-91.

1339. Sherman, K.J., et al., *Effectiveness of therapeutic massage for generalized anxiety disorder: a randomized controlled trial.* Depress Anxiety, 2010. **27**(5): p. 441-50.

1340. Robinson, J., F.C. Biley, and H. Dolk, *Therapeutic touch for anxiety disorders.* Cochrane Database of Systematic Reviews, 2007(3).

1341. Gomes, V.M., M. Silva, and E. Araujo, *Gradual effects of therapeutic touch in reducing anxiety in university students.* Revista brasileira de enfermagem, 2008. **61**(6): p. 841-846.

1342. Lee, M.S., M.H. Pittler, and E. Ernst, *Effects of reiki in clinical practice: a systematic review of randomised clinical trials.* International journal of clinical practice, 2008. **62**(6): p. 947-954.

1343. Anderson, J.G. and A.G. Taylor, *Effects of healing touch in clinical practice: a systematic review of randomized clinical trials.* Journal of Holistic Nursing, 2011. **29**(3): p. 221-228.

1344. Kandola, A., et al., *Moving to beat anxiety: epidemiology and therapeutic issues with physical activity for anxiety.* Current psychiatry reports, 2018. **20**(8): p. 63.

1345. Vieira, Á., et al., *Virtual reality exercise on a home-based phase III cardiac rehabilitation program, effect on executive function, quality of life and depression, anxiety and stress: a randomized controlled trial.* Disability and Rehabilitation: Assistive Technology, 2018. **13**(2): p. 112-123.

1346. Abuse, N.I.o.D. *Overdose Death Rates*. 2020; Available from: https://www.drugabuse.gov/drug-topics/trends-statistics/overdose-death-rates.

1347. R, P., *The ASAM essential of addiction medicine.* 2015: p. 53-54.

1348. Fontaine, R., et al., *Comparison of withdrawal of busiprone and diazepam: A placebo controlled study.* Progress in neuro-psychopharmacology & biological psychiatry, 1987.

1349. Murphy, S.M., R. Owen, and P. Tyrer, *Comparative assessment of efficacy and withdrawal symptoms after 6 and 12 weeks' treatment with diazepam or buspirone.* The British Journal of Psychiatry, 1989. **154**(4): p. 529-534.

1350. Rickels, K., et al., *Clorazepate and lorazepam: clinical improvement and rebound anxiety.* Am J Psychiatry, 1988. **145**(3): p. 312-7.

1351. Busto, U., et al., *Withdrawal reaction after long-term therapeutic use of benzodiazepines.* N Engl J Med, 1986. **315**(14): p. 854-9.

1352. Hood, S.D., et al., *Benzodiazepine dependence and its treatment with low dose flumazenil.* British journal of clinical pharmacology, 2014. **77**(2): p. 285-294.

1353. Greenberg, M.I.M.D., *Benzodiazepine Withdrawal: Potentially Fatal, Commonly MissedFollowing benzodiazepine cessation, withdrawal symptoms may begin within 24 hours or take up to two weeks to develop.* Emergency Medicine News, 2001. **23**(12).

1354. Lann, M.A. and D.K. Molina, *A fatal case of benzodiazepine withdrawal.* The American journal of forensic medicine and pathology, 2009. **30**(2): p. 177-179.

1355. CPSA. *Benzodiazepines: Use and Taper*. 2016; Available from: https://cpsa.ca/wp-content/uploads/2020/06/AP_Prescribing-Drugs-Associated-with-Substance-Use-Disorders.pdf.

Copyright ©2021 Reed Group, Ltd.

1356. Hughes, M.A., et al., *Recommended Opioid Prescribing Practices for Use in Chronic Non-Malignant Pain: A Systematic Review of Treatment Guidelines.* Journal of Managed Care Medicine, 2011. **14**(3).

1357. Shah, N.G., et al., *Unintentional drug overdose death trends in New Mexico, USA, 1990–2005: combinations of heroin, cocaine, prescription opioids and alcohol.* Addiction, 2008. **103**(1): p. 126-136.

1358. Baillargeon, L., et al., *Discontinuation of benzodiazepines among older insomniac adults treated with cognitive-behavioural therapy combined with gradual tapering: a randomized trial.* Canadian Medical Association Journal, 2003. **169**(10): p. 1015.

1359. Rickels, K., et al., *Imipramine and buspirone in treatment of patients with generalized anxiety disorder who are discontinuing long-term benzodiazepine therapy.* American Journal of Psychiatry, 2000. **157**(12): p. 1973-1979.

1360. Welsh, J.W., et al., *Adjunctive pharmacologic approaches for benzodiazepine tapers.* Drug and alcohol dependence, 2018. **189**: p. 96-107.

1361. Dou, C., J. Rebane, and S. Bardal, *Interventions to improve benzodiazepine tapering success in the elderly: a systematic review.* Aging & mental health, 2019. **23**(4): p. 411-416.

1362. Takaesu, Y., et al., *Psychosocial intervention for discontinuing benzodiazepine hypnotics in patients with chronic insomnia: a systematic review and meta-analysis.* Sleep medicine reviews, 2019. **48**: p. 101214.

1363. Otto, M.W., et al., *Discontinuation of benzodiazepine treatment: efficacy of cognitive-behavioral therapy for patients with panic disorder.* Am J Psychiatry, 1993. **150**(10): p. 1485-90.

1364. Lader, M. and A. Kyriacou, *Withdrawing benzodiazepines in patients with anxiety disorders.* Current psychiatry reports, 2016. **18**(1): p. 8.

1365. Baandrup, L., et al., *Pharmacological interventions for benzodiazepine discontinuation in chronic benzodiazepine users.* Cochrane Database of Systematic Reviews, 2018(3).

1366. Yeung, W.F., et al., *Electroacupuncture for tapering off long-term benzodiazepine use: A randomized controlled trial.* J Psychiatr Res, 2019. **109**: p. 59-67.

1367. Ashton, C., *Benzodiazepines: how they work & how to withdraw (aka The Ashton Manual).* Newcastle, England: University of Newcastle, 2002.

1368. Busse, J.W., et al., *Guideline for opioid therapy and chronic noncancer pain.* Canadian Medical Association Journal, 2017. **189**(18): p. E659-E666.

1369. Hadley, S.J., F.S. Mandel, and E. Schweizer, *Switching from long-term benzodiazepine therapy to pregabalin in patients with generalized anxiety disorder: a double-blind, placebo-controlled trial.* Journal of Psychopharmacology, 2012. **26**(4): p. 461-470.

1370. Brett, J. and B. Murnion, *Management of benzodiazepine misuse and dependence.* Aust Prescr, 2015. **38**(5): p. 152-5.

1371. Fluyau, *Re-evaluating the use of benzodiazepines.* Payne Current psychiatry, 2018. **18**(3): p. 9-10.

1372. Vicens, C., et al., *Comparative efficacy of two interventions to discontinue long-term benzodiazepine use: cluster randomised controlled trial in primary care.* The British Journal of Psychiatry, 2014. **204**(6): p. 471-479.

1373. Vicens, C., et al., *Efficacy of two interventions on the discontinuation of benzodiazepines in long-term users: 36-month follow-up of a cluster randomised trial in primary care.* Br J Gen Pract, 2016. **66**(643): p. e85-91.

1374. Romach, M.K., et al., *A controlled trial of ondansetron, a 5-HT3 antagonist, in benzodiazepine discontinuation.* J Clin Psychopharmacol, 1998. **18**(2): p. 121-31.

Copyright ©2021 Reed Group, Ltd.

1375. Cassano, G., et al., *A randomized, double-blind study of alpidem vs placebo in the prevention and treatment of benzodiazepine withdrawal syndrome.* European psychiatry, 1996. **11**(2): p. 93-99.

1376. Mercier-Guyon, C., J. Chabannes, and P. Saviuc, *The role of captodiamine in the withdrawal from long-term benzodiazepine treatment.* Current medical research and opinion, 2004. **20**(9): p. 1347-1355.

1377. Lemoine, P., et al., *Double-blind, comparative study of cyamemazine vs. bromazepam in the benzodiazepine withdrawal syndrome.* Progress in Neuro-Psychopharmacology and Biological Psychiatry, 2006. **30**(1): p. 131-137.

1378. Klein, E., et al., *Alprazolam withdrawal in patients with panic disorder and generalized anxiety disorder: vulnerability and effect of carbamazepine.* The American journal of psychiatry, 1994.

1379. Rynn, M., et al., *Imipramine and buspirone in patients with panic disorder who are discontinuing long-term benzodiazepine therapy.* Journal of clinical psychopharmacology, 2003. **23**(5): p. 505-508.

1380. Otto, M.W., et al., *Efficacy of CBT for benzodiazepine discontinuation in patients with panic disorder: Further evaluation.* Behav Res Ther, 2010. **48**(8): p. 720-7.

1381. Rickels, K. and E. Schweizer, *Panic disorder: Long-term pharmacotherapy and discontinuation.* Journal of Clinical Psychopharmacology, 1998. **18**(6 SUPPL. 2): p. 12S-18S.

Copyright ©2021 Reed Group, Ltd.