

Anxiety Disorders in Older Adults

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Faculty

Beyon Miloyan, PhD, received his PhD in Psychology from the University of Queensland in 2015 for his thesis on late-life anxiety disorders. He completed his postdoctoral training in the Epidemiology and Biostatistics of Aging program at the Johns Hopkins University before taking a tenure-track position in the School of Psychology and Health Sciences at Federation University, Australia. Dr. Miloyan has published 30 peer-reviewed journal articles and book chapters and has been teaching since 2012. He has supervised 10 student theses at doctoral, Master's, and undergraduate levels and served as an ad hoc peer reviewer for various journals in the fields of psychology, psychiatry, and public health.

Faculty Disclosure

Contributing faculty, Beyon Miloyan, PhD, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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The division planners and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Audience

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Course Objective

Older adults are the fastest growing demographic in the world, and anxiety disorders are the most common mental disorder in this age group. The purpose of this course is to provide clinicians with the knowledge and skills necessary in order to improve the assessment and treatment of anxiety disorders in older adults.

Learning Objectives

Upon completion of this course, you should be able to:

1. Describe the history and neuroanatomy of anxiety and anxiety disorder.
2. Discuss the assessment and classification of anxiety disorders in older adults.
3. Analyze the epidemiology of anxiety disorders in elderly patients.
4. Describe the clinical implications of late-life anxiety disorders and their treatment.



EVIDENCE-BASED
PRACTICE
RECOMMENDATION

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

The first known clinical case description of an anxiety disorder appeared in the medical corpus of the Ancient Greek physician Hippocrates. The description tells of Nicanor, a man who developed an extreme fear of a “flute girl” whom he encountered one night at a drinking party and who haunted him every night for many years. Five hundred years after this case description, the Ancient Roman Stoic philosophers Seneca the Younger and Cicero addressed the topic of anxiety at length, recognizing both its benefits and harms, depending on the severity and circumstances of the anxiety [1]. These texts reveal a sophisticated understanding of fear and anxiety among these ancient authors, even by modern medical standards. It was not until the 19th century that Charles Darwin noted essential similarities in the expression of fear and anxiety in mammals, reinforcing Seneca’s notion that fear and anxiety are ultimately adaptive traits [2]. In its normal state, anxiety facilitates the management of potential future hazards [3; 4; 5]. In its extreme state, the individual regards it as excessive or distressing or it can cause impairment in the individual’s daily life, thus constituting a disorder [6; 7].

The analogy of a smoke detector demonstrates the adaptive and maladaptive aspects of anxiety [8; 9]. Just as the function of a smoke detector is to signal potential fires so that one can take action to prevent harm, the function of anxiety is to signal any potential hazards so that preventive actions can be taken. In this analogy, an anxiety disorder is an extreme that renders the individual more sensitive to threat signals [10]. Although those with higher anxiety experience more false alarms (signals for a threat that does not occur), this is advantageous to the extent that it reduces the risk of a fatal miss. In other words, the costs associated with false alarms and misses are not equal: over-reacting to non-threats is generally less costly than failing to detect one danger. Nonetheless, living in a chronic state of high anxiety can take a long-term toll on an individual’s health and quality of life, and in these cases, intervention is warranted.

Age-related changes in anxiety can occur over the course of one’s life, and understanding these changes is key to facilitating clinical detection and treatment, particularly among older adults, who are the largest and fastest-growing age demographic in the United States. This course begins by addressing the neuroanatomy of anxiety, followed by its classification and a review of commonly used methods of assessment. The course goes on to cover the epidemiology of anxiety disorders in older adults, including its prevalence, incidence, course, risk factors, and consequences. Finally, treatment considerations are addressed.

NEUROANATOMY

In 1949, the Nobel Prize in Medicine was awarded to António Egas Moniz for his discovery of “a simple operation, always safe, [and] which may prove to be an effective surgical treatment in certain cases of mental disorder” [11]. Specifically, Moniz discovered the prefrontal leukotomy as a treatment for mental disorders, including anxiety disorders [12]. Since then, studies have found that damage to the ventromedial prefrontal cortex produces resistance against anxiety and depression [13; 14; 15; 16]. Despite the effective reduction of anxiety in these patients, it took many decades until research began to address the harms imposed by damage to the prefrontal cortex. For example, in addition to reducing anxiety, damage to the ventromedial prefrontal cortex also impairs self-regulation and decision-making and can induce sociopathic behaviors [17; 18; 19; 20; 21]. Similar patterns of anxiety reduction were also observed in one patient with focal bilateral lesions to the amygdalae who showed a similar pattern of impairment in her daily life as those with damage to the prefrontal cortex [22]. Although the prefrontal cortex and amygdala are critical structures in a neural network that is necessary for anxiety, these findings highlight the fact that damage to these structures comes with unintended consequences.

These findings also highlight the more general point that, in treating anxiety disorders, it is also important to not abolish otherwise useful traits as it is to reduce the anxiety to a manageable level.

CLASSIFICATION

The *Diagnostic and Statistical Manual of Mental Disorders* (DSM) sub-classifies anxiety disorders into panic disorder, agoraphobia, specific phobia, social anxiety disorder, and generalized anxiety disorder (GAD) [6]. In the following sections, each of these subtypes are described, including the relevant criteria for diagnosis and a description of age-related differences in symptom patterns. The most frequently reported symptom(s) for each disorder in older adults are based on data from the National Epidemiological Survey on Alcohol and Related Conditions (NESARC).

PANIC DISORDER AND AGORAPHOBIA

Panic disorder is characterized by the occurrence of panic attacks. Panic attacks are defined as sudden, unexpected, and brief onsets of terror, accompanied by at least four of the following symptoms: sweating, trembling, chest pain, dizziness, nausea, chills or hot flashes, numbness or tingling, shortness of breath or choking, a feeling of loss of control, desensitization, or a fear of death. In order to be classified as panic disorder, the DSM requires such panic attacks to be accompanied by a period of at least one month in which the individual also fears the possibility of a future panic attack [6].

Two main subtypes of panic disorder have been observed, diverging between individuals with respiratory and non-respiratory symptoms [23; 24; 25]. Determining the subtype may be informative for treatment purposes. Older adults with panic disorder experience fewer symptoms of panic compared with younger adults, and their panic attacks are also reported to be less intense and shorter in duration [26; 27; 28; 29].

Agoraphobia is characterized by a fear or avoidance of situations from which escape is difficult. The diagnosis requires a fear or avoidance of two or more of the following specific situations: public transportation, open spaces, closed spaces, crowds, or being alone in public. Although the presence of these fears is also associated with panic disorder and specific phobia, a distinguishing factor of agoraphobia is defined by the frequency of the aforementioned fears. Individuals with greater and more frequent occurrences of these fears tend to be classified as having agoraphobia [30].

Table 1 displays the most commonly reported panic symptoms among older adults (55 years of age and older) with a diagnosis of panic disorder (with or without agoraphobia). The total percentage of each symptom is displayed. The prevalence of panic disorder in this sample was 1.2% (95% confidence interval [CI]: 1.0–1.5).

SPECIFIC PHOBIA

The central feature of specific phobia is the fear or avoidance of specific objects or situations. These include, but are not limited to, animals (e.g., snakes or insects), the natural environment (e.g., storms, water, or heights), situations (e.g., typically closed or open spaces), and blood, injections, or injury. A diagnosis of specific phobia requires the individual to recognize that the fear or avoidance is unreasonable and to regard it as distressing or interfering with their everyday life. The most common fears reported by adults involve animals, heights, and flying [32; 33; 34]. However, older adults frequently report situational fears [35]. Individuals who report having at least one specific fear are likely to report having other fears [33; 36].

Table 2 displays the most commonly reported specific fears among older adults (55 years of age and older) with a diagnosis of specific phobia. The prevalence of specific phobia in this sample was 5.5% (95% CI: 5.0–6.0).

PREVALENCE OF PANIC SYMPTOMS AMONG OLDER ADULTS WITH PANIC DISORDER			
Symptom	Age Groups		
	55 to 64 Years	65 Years and Older	55 Years and Older
Shortness of breath	82%	85%	83%
Heart racing/pounding	91%	82%	88%
Trembling/shaking	73%	69%	72%
Perspiring/sweating	75%	65%	72%
Felt as if choking	45%	57%	50%
Dizzy/lightheaded	74%	74%	74%
Things seemed unreal	61%	56%	59%
Tingling/numbness	57%	50%	54%
Flushes/hot flashes/chills	71%	53%	64%
Nauseous/upset stomach	50%	56%	53%
Pain/pressure in chest	63%	56%	60%
Going crazy/losing control	63%	61%	62%
Felt might die	58%	64%	60%

Source: [31] Table 1

PREVALENCE OF SPECIFIC FEARS AMONG OLDER ADULTS WITH SPECIFIC PHOBIA				
Object of Fear/ Avoidance	Age Groups			
	55 to 64 Years	65 to 74 Years	75 Years and Older	55 Years and Older
Animals	57%	56%	62%	58%
Heights	53%	60%	49%	55%
Storms	26%	30%	45%	31%
Being in/on water	31%	41%	45%	37%
Flying	35%	36%	33%	35%
Crowds/lines	13%	12%	23%	15%
Closed spaces	40%	38%	41%	40%
Blood/injections	16%	11%	17%	15%
Public transportation	9%	6%	7%	7%
Going to the dentist	31%	32%	27%	30%
Hospitals	15%	12%	17%	15%

Source: [31] Table 2

PREVALENCE OF SOCIAL ANXIETY SYMPTOMS AMONG OLDER ADULTS WITH SOCIAL ANXIETY DISORDER			
Symptom	Age Groups		
	55 to 64 Years	65 Years and Older	55 Years and Older
Social situations made you nervous	81%	85%	83%
Social situations made you upset/anxious	93%	93%	93%
Endured social situations that frightened you	88%	85%	87%
Avoided social situations out of strong fear	82%	72%	77%
More frightened in social situations than most people	80%	76%	78%
Thought fear of social situations stronger than it should be	92%	89%	90%
Had a panic attack in social situations	22%	8%	15%
Frightened of social situations out of fear of panic attack	16%	8%	12%
Remained in social situation despite fear of panic attack	20%	11%	15%

Source: [31]

Table 3

SOCIAL ANXIETY DISORDER

The core feature of social anxiety disorder is the fear or avoidance of social situations. The fear or avoidance concerns the possibility of negative judgment by others (e.g., resulting in embarrassment or humiliation). Social anxiety may pertain to particular types of social settings or situations, such as small or large group settings, or the anxiety may generalize to a variety of social situations. Older adults endorse fewer social anxiety symptoms relative to younger adults [37]. The most common social fears among older adults include public speaking or being confronted or criticized by others, while discomfort with and avoidance of social situations and experiencing anxiety when thinking about social situations appears equally common to both younger and older adults [37; 38].

Table 3 displays the most commonly reported social fears among older adults (55 years of age and older) with a diagnosis of social anxiety disorder. The prevalence of social anxiety disorder in this sample was 2.0% (95% CI: 1.7–2.3).

GENERALIZED ANXIETY DISORDER

The central feature of GAD is intrusive worry, defined as repetitive thinking about potentially harmful future events. Worries generally pertain to everyday concerns and involve attempts to minimize the likelihood or consequences of disadvantageous outcomes. Although some degree of worry is recognized as helpful, when the individual reports experiences of excessive and uncontrollable worry for a period of six months or more, this constitutes a diagnosis of GAD if, and only if, the worry is also regarded by the individual as causing distress or impairment [39]. Age-related reductions in worry frequency have been observed in older adult samples from the United States, United Kingdom, Canada, and Australia [40; 41; 42; 43; 44; 45; 46]. There are also age-related differences in the subjects of individuals' worries. For example, for younger adults, common worries concern work, finances, and personal relationships. For older adults, these concerns give way to worries about personal health and the health and welfare of loved ones [41; 44; 46]. These "world issue" worries typically focus outwardly on problems that could

PREVALENCE OF GENERALIZED ANXIETY DISORDER SYMPTOMS AMONG OLDER ADULTS WITH GENERALIZED ANXIETY DISORDER			
Symptom	Age Groups		
	55 to 64 Years	65 Years and Older	55 Years and Older
Worry a lot about things you usually didn't worry about?	83%	72%	78%
Ever think your worrying was excessive?	56%	47%	52%
Often got tired easily	83%	81%	82%
Often had tense, sore, aching muscles	76%	67%	71%
Became so restless you paced, fidgeted, or could not sit still	62%	55%	58%
Often felt keyed up or on edge	82%	78%	80%
Often had trouble concentrating	83%	83%	83%
Often felt irritable	80%	62%	71%
Often had trouble falling/staying asleep	77%	72%	74%
Often forgot what you were talking about/ mind went blank	75%	66%	70%
Often felt heart racing, skipping, or pounding in chest	59%	45%	52%
Often perspired/sweated	50%	35%	43%
Often had cold and clammy hands	44%	27%	36%
Often had dry mouth	58%	49%	54%
Often felt dizzy/lightheaded/like might faint	48%	53%	50%
Often felt nauseous	54%	34%	45%
Often urinated frequently	54%	47%	51%
Often had trouble swallowing/felt like lump in throat	37%	34%	35%
Often had pain/pressure in chest	40%	31%	36%
Often trembled/shook	34%	39%	36%
Often had trouble catching breath/felt like smothering	43%	33%	39%

Source: [31]

Table 4

be faced by future generations, which may be of particular relevance during this developmental life stage [43]. In fact, late-life developmental transitions have been associated with other context-specific worries, such as concerns of becoming a burden after transitioning out of a primary caregiver role and into retirement [47; 48]. Caregiving, too, can be a significant source of worry, anxiety, and distress in later life [49; 50; 51]. Older adults

who report financial worries tend to be concerned about receiving care and about their own capacity to make decisions [52]. However, despite the observation that older adults with GAD tend to endorse a greater variety of worries than matched non-GAD controls, there are fewer differences in the experience of worry between older adults with and without GAD than there are between younger adults with and without GAD [53; 54].

In essence, the expression of worry may vary significantly as a function of the developmental stage of the individual, with older adults endorsing worries commensurate with their changing life circumstances [55].

Table 4 displays the most commonly reported generalized anxiety disorder symptoms among older adults (55 years of age and older) with a diagnosis of GAD. The prevalence of GAD in this sample was 2.0% (95% CI: 1.7–2.3).

ASSESSMENT

STRUCTURED AND SEMI-STRUCTURED INTERVIEWS

The standard procedure for anxiety disorder assessment is the structured diagnostic interview, which is administered by a trained professional. The structured interview consists of pre-determined questions that assess for relevant symptoms based on diagnostic criteria. For example, an interview for GAD would start by asking the individual questions about the presence of worry symptoms over the past six months. If the interviewee answers this question affirmatively, the interviewer would then ask the individual about the presence of secondary symptoms associated with the worry (e.g., sleep, irritability). If the individual responds affirmatively to the minimum number of secondary symptoms required for a diagnosis of GAD, the individual would then be queried about the presence of distress or impairment due to the worry. The key advantage of the structured interview is its standardized administration, procedure, and scoring, which minimize bias and error in assessment. Two commonly used structured interviews for the assessment of mental disorders are the Diagnostic Interview Schedule (DIS) and the Composite International Diagnostic Interview (CIDI) [56; 57]. In addition, the Anxiety Disorders Interview Schedule (ADIS) is a structured diagnostic interview that was developed specifically for anxiety disorder assessment [58]. These interviews are regularly updated along with diagnostic criteria, as

for example with new editions of the DSM. Structured interviews rely essentially on self-report; in addition to being administered by clinicians, they may also be conducted by trained lay persons and/or computer-assisted technology (as in epidemiologic surveys).

The examination modality of assessment contrasts with the interview technique in that the person conducting the assessment, typically a trained clinician, decides about the presence or absence of a symptom instead of relying on the report of the individual. The Structured Clinical Interview for the DSM (SCID) and the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) are examples of semi-structured interviews/examinations that allow the clinician to take a more flexible approach to the interview while retaining some degree of structure [59; 60]. Structured interviews and semi-structured examinations are not always practical to use because they are time-consuming to administer. Nonetheless, they are essential for validating briefer, easier to administer, and more widely used questionnaires and screening tools for use in particular contexts.

As a result of the evolving racial and immigration demographics in the United States, interaction with patients for whom English is not a native language is inevitable. Because diagnosing anxiety disorders is reliant on good communication, it is each practitioner's responsibility to ensure that interviews and assessments are conducted in such a way that allows for patient understanding. When there is an obvious disconnect in the communication process between the practitioner and patient due to the patient's lack of proficiency in the English language, an interpreter is required.

Mental health professionals should consider undertaking a language needs analysis for the service population and consider how to best meet identified needs. If possible, 10 to 15 minutes should be reserved in advance of sessions to brief the interpreter about the purpose of the meeting and to enable them to explain any cultural issues that may have bearing on the session.

RATING SCALES

Generalized Anxiety Disorder

The Generalized Anxiety Disorder 7-item (GAD-7) scale is a brief, self-administered screening instrument for use in medical settings. The scale assesses for symptoms occurring over the previous two weeks of the respondent's life [61; 62]. Each item is rated on a four-point scale (0 to 3) yielding a maximum score of 21. A score of 10 or greater indicates a probable diagnosis of GAD based on validation against the psychiatrist-administered SCID [62]. There is also a shorter, two-item version called the GAD-2. The GAD-7 (along with scoring instructions) can be accessed online at https://adaa.org/sites/default/files/GAD-7_Anxiety-updated_0.pdf. The GAD-2 consists of only the first two items of the GAD-7, with scores of 3 or greater indicating clinically significant anxiety symptoms [63].

Panic Disorder

The Panic Disorder Severity Scale (PDSS) is a brief, self-administered screening instrument [64]. There are seven items, each rated on a five-point scale (0 to 4) yielding a maximum score of 28. A score of eight or greater indicates a probable diagnosis of panic disorder based on validation against the ADIS or the psychiatrist-administered SCID [65]. The PDSS and scoring instructions can be accessed online at <http://www.goodmedicine.org.uk/files/panic,%20assessment%20pdss.pdf>.

Social Anxiety Disorder

The Social Phobia Inventory (SPIN) is a self-administered screening instrument [66]. There are 17 items, each rated on a five-point scale (0 to 4), yielding a total score of 68. A score of 19 or greater indicates a probable diagnosis of social anxiety disorder. There also a shorter, three-item version called the Mini-SPIN [67; 68]. The SPIN and its scoring instructions can be accessed online at http://www.goodmedicine.org.uk/files/social%20anxiety,%20assessment%20spin.full_.tahoma_0.pdf.

Specific Phobia/Agoraphobia

There are currently no validated rating scales for the assessment of specific phobia or agoraphobia. However, screening for specific phobia is simpler than for other anxiety subtypes. The clinician starts by assessing whether the individual has a fear or avoidance of any specific stimulus or situation. If the individual answers affirmatively, then the clinician assesses whether the fear/avoidance is regarded as excessive or unreasonable and whether it interferes with the individual's life. Both criteria must be met for a patient to screen positive.

General (Transdiagnostic) Anxiety Screening

The Overall Anxiety Severity and Impairment Scale (OASIS) is a brief, transdiagnostic screening tool designed to assess for the severity of anxiety in the past week of the individual's life [69]. There are five items, each rated on a five-point scale (0 to 4), yielding a total possible score of 20. A raw score of 8 or greater indicates the presence of anxiety disorder based on validation against anxiety disorder diagnosis using the psychiatrist-administered SCID [70]. Raw scores of 10 and 12 indicate the presence of marked and severe anxiety, respectively, based on validation against the clinician-rated Clinical Global Impression-Severity (CGI-S) scale in a sample of individuals with any anxiety disorder ascertained using the Mini International Neuropsychiatric Interview (MINI) [71].

Scales for Older Adult/Geriatric Use

The Geriatric Anxiety Inventory (GAI) is a 20-item questionnaire designed specifically for older adults (65 years of age and older) [72; 73]. It is a self-report or clinician-administered measure, with each item rated on a binary response scale (agree/disagree), for a total score of 20. Scores of 10 or greater indicate a probable diagnosis of anxiety disorder. The GAI has been translated to more than 20 languages. The GAI has also been validated in clinical and non-clinical samples and in those with cognitive impairment and Parkinson disease [74; 75; 76]. There is also a five-item version called the Geriatric Anxiety Inventory-Short Form (GAI-SF) [77]. Both versions can be accessed online at <http://gai.net.au>.

The Geriatric Anxiety Scale (GAS) is a self-report questionnaire designed for use among adults 65 years of age and older [78]. The GAS contains 30 items, of which only 25 are used to derive a total score. The remaining five questions are used to help the clinician identify areas of concern for the respondent. Each item is rated on a four-point scale (from 0 to 3), yielding a total score of 100. The GAS consists of three sub-scales assessing somatic (9 items, total possible score: 36), cognitive (8 items, total possible score: 32), and affective (8 items, total possible score: 32) symptoms. There is also a shorter, 10-item version called the GAS-10 [79]. The standard GAS can be accessed at https://gerocentral.org/wp-content/uploads/2013/03/Geriatric-Anxiety-Scale-v2.0_FINAL.pdf, and the GAS-10 can be accessed at <https://gerocentral.org/wp-content/uploads/2013/03/GAS-10-item-version-2015-1-15.pdf>.

Assessment Implications

Compared with younger adults, older adults report fewer and less concrete anxiety symptoms across anxiety subtypes [40; 41; 42; 43; 45]. In addition to this, age-related neurocognitive impairment makes self-reporting a more difficult method of assessment [55]. For example, those with memory impairment can experience stressors that evoke negative effects without leaving memory traces [22; 80]. Although informant report can be a way of effectively gathering information about observable (e.g., physical) symptoms, it is ineffective for identifying unobservable (i.e., subjective) symptoms [81].

EPIDEMIOLOGY

This section addresses the epidemiology of anxiety disorders in older adults, which focuses on the occurrence, determinants, and course and consequences of anxiety disorders in the population. The focus is on the U.S. population, using data from nationally representative surveys. The section begins by addressing the occurrence of anxiety disorders by describing their prevalence and incidence. It then addresses the course and

consequences of anxiety disorder, which includes their chronicity, persistence, and comorbidity. Finally, the determinants of anxiety disorders are explored by focusing on risk factors.

PREVALENCE

Prevalence is an estimate of the percent of individuals in the population who meet diagnostic criteria for anxiety disorder, either overall or by subtype. While lifetime prevalence estimates are concerned with the presence of anxiety disorders within the lifetime of individuals, these estimates are typically unreliable because they require respondents to recall prior episodes of anxiety and associated symptoms [82]. Estimating lifetime prevalence in older adults is particularly unreliable, due to general age-related memory deficits [83]. In contrast to lifetime prevalence, period prevalence estimates focus on the presence of anxiety disorder within a given timeframe, typically 12 months. The data in this section are one-year prevalence estimates of anxiety disorder (i.e., whether anxiety disorders were present or absent in the past year of respondents' lives) in nationally representative samples of the U.S. population.

Anxiety disorders are the most prevalent mental disorders in older adults [54; 84]. The most prevalent subtypes are, in descending order, specific phobia, GAD, social anxiety disorder, and panic disorder. **Table 5** displays the one-year prevalence of anxiety disorders, both overall and by subtype, in the NESARC and the Collaborative Psychiatric Epidemiology Surveys (CPES) of the United States. The prevalence of anxiety disorders is higher among women relative to men, and the prevalence of all anxiety subtypes decreases among persons 75 years of age or older. Previous studies have also reported ethnic differences in prevalence, such that Native and White Americans have the highest prevalence, and Hispanic and Asian Americans have the lowest prevalence of anxiety disorders [85]. Black Americans have a higher or lower prevalence of anxiety disorders depending on subtype; specific phobias and GAD are more prevalent, comparable to Native and White Americans, whereas panic disorder and social anxiety disorder

ONE-YEAR PREVALENCE OF ANXIETY DISORDER AMONG ADULTS 55 YEARS OF AGE AND OLDER IN TWO NATIONAL SAMPLES										
Population	Specific Phobia		Social Anxiety Disorder		Generalized Anxiety Disorder		Panic Disorder		Any Anxiety Disorder	
	NESARC	CPES ^a	NESARC	CPES	NESARC	CPES	NESARC	CPES	NESARC	CPES ^b
Total	5%	6%	2%	3%	1%	3%	1%	2%	9%	6%
Age (years)										
55–64	6%	8%	3%	5%	2%	4%	2%	2%	11%	9%
65–74	5%	5%	2%	3%	1%	2%	1%	1%	8%	4%
75+	3%	4%	1%	1%	1%	15%	1%	2%	6%	4%
Sex										
Male	4%	4%	2%	2%	1%	2%	1%	1%	6%	5%
Female	7%	7%	2%	4%	2%	3%	2%	2%	11%	7%
Education										
Less than high school	6%	10%	3%	4%	2%	3%	2%	2%	9%	7%
Completed high school	6%	5%	2%	3%	1%	2%	1%	1%	9%	5%
Some college	6%	6%	2%	3%	2%	4%	1%	2%	9%	9%
Bachelor's degree	4%	4%	1%	2%	1%	2%	1%	1%	7%	5%
Marital status										
Married or cohabiting	5%	5%	2%	2%	1%	2%	1%	1%	8%	4%
Widowed, divorced or separated	6%	8%	2%	5%	2%	4%	2%	2%	10%	9%
Never married	5%	7%	2%	6%	2%	2%	1%	2%	9%	7%
^a Specific phobia was assessed in a sub-sample of 9,282 respondents from the NCS-R.										
^b Specific phobia was not included in the overall anxiety disorder estimate for the CPES.										
Source: [31; 84]										Table 5

are less prevalent, closer to levels observed in Hispanic and Asian Americans. The prevalence of anxiety disorders does not vary substantially by educational attainment or marital status.

INCIDENCE

The incidence of a disease is defined as the rate at which new cases occur. In contrast to prevalence estimates, which are based on single diagnostic assessments, incidence estimates require at least two diagnostic assessments. The reason for this is that anyone meeting criteria for an anxiety disorder at any time is counted as a case for the purpose of prevalence estimation, whereas only those individuals who did not have anxiety disorder at time one and who went on to be diagnosed with anxiety disorder at time two are counted as cases for the purpose of incidence estimation, showing that the individuals represent new occurrences of the disorder. The individuals at time one who do not meet criteria for an anxiety disorder are

the “risk set” and form the denominator of the incidence ratio, and the individuals at time two or later who meet criteria for an anxiety disorder form the numerator over the period in which the diagnostic assessments were made.

Just as the prevalence of anxiety disorder is higher in older adults than other mental disorders, so too is the incidence, or the rate of newly diagnosed cases [86]. The subtypes with the highest incidence, in descending order, are specific phobia, social anxiety disorder, panic disorder, agoraphobia, and GAD [87; 88]. Data from the Epidemiologic Catchment Area (ECA) study and National Comorbidity Survey (NCS) in the United States, and the Netherlands Mental Health Survey and Incidence Study (NEMESIS) indicate that women have a higher incidence than men [88; 89]. Although anxiety disorder often peaks in young adulthood, there is a smaller but important second peak that occurs in older adulthood [88; 89].

COURSE

The chronicity of a disease refers to its persistence. Persistence is defined here as the percentage of respondents who meet diagnostic criteria for an anxiety disorder at baseline and who then meet criteria again at follow-up. Data from the NESARC indicate that approximately 30% of older adults (55 years of age and older) have persistent cases of anxiety disorder, or chronicity, assessed over a three-year follow-up period. The most persistent subtypes were specific phobia (25%) and GAD (20%), followed by social anxiety disorder (16%) and panic disorder (10%) [31].

There is high co-occurrence between anxiety and other mental disorders, particularly major depression [90; 92; 93]. Panic disorder and GAD have a particularly high comorbidity with mood and substance use disorders in adults [94]. Specific phobia has a strong association with social anxiety disorder and depression [95]. Finally, there are strong associations between social anxiety disorder, GAD, and bipolar disorder [91]. These patterns generally persist among older adults [54]. Anxiety subtypes also have high degrees of overlap [91; 94; 95].



EVIDENCE-BASED
PRACTICE
RECOMMENDATION

When assessing an adult with possible social anxiety disorder, the National Collaborating Centre for Mental Health recommends that clinicians be aware of comorbid disorders, including avoidant personality disorder, alcohol and substance misuse, mood disorders, other anxiety disorders, psychosis, and autism.

(<https://www.nice.org.uk/guidance/cg159/resources/social-anxiety-disorder-recognition-assessment-and-treatment-pdf-35109639699397>. Last accessed February 17, 2022.)

Level of Evidence: Expert Opinion/Consensus Statement

Data from the National Comorbidity Survey (NCS) suggest that anxiety disorders are also associated with various physical conditions [96]. While panic attacks are associated with vascular conditions, specific phobias are linked with respiratory conditions, and social anxiety disorder with metabolic conditions. Among older adults, there are high rates of anxiety disorders in individuals who have chronic obstructive pulmonary disease (COPD) and/or cardiovascular diseases [35; 97]. The Baltimore ECA study reports an association between blood-injection phobia and vascular complications among individuals with diabetes, which suggests the possibility that fear of blood and injections may interfere with medical treatment [98]. Blood-injection phobia is also associated with respiratory conditions, similar to the data on overall phobias in the NCS sample [99]. The prevalence of blood-injection phobia ranges from 4% to 8% in older adults [36; 100].

CONSEQUENCES

As discussed, anxiety is diagnosed as a disorder only when it is deemed by the individual to be a cause of distress and/or to interfere with daily life. In the NEMESIS study, those with anxiety disorder at baseline had more suicidal ideation and suicide attempts at three-year follow-up, after adjustment for demographic characteristics and past history of mental disorders [101]. Similar associations were observed in cross-sectional studies of the NESARC and NCS-R samples of adults residing in the United States [102].

Importantly, the findings of a 2016 systematic review and meta-analysis of prospective, longitudinal studies suggest that a diagnosis of any anxiety disorder at baseline is not associated with increased risk of all-cause mortality at follow-up [5]. In fact, in a population study of Norwegians, high anxiety symptoms were associated with lower mortality among individuals with depression [103]. In a population study of a 1946 UK birth cohort, individuals who demonstrated lower levels of trait anxiety in adolescence were associated with higher

risk of accident mortality at follow-up [104]. Thus, low anxiety (but not high anxiety) is associated with increased mortality risk, and some degree of anxiety is beneficial for survival. Some anxiety likely encourages individuals to engage in preventive health behaviors. For example, women who worry about the possibility of breast cancer are more likely to seek routine screenings, people who are more worry-prone are more likely to vaccinate than those who worry less, and smokers with higher worries about their health have been found to be more likely to quit [105; 106; 107].

RISK FACTORS, RISK ASSESSMENT, AND PREVENTION

The two strongest risk factors for anxiety disorders among older adults are female sex and younger age [84; 108; 109]. However, other risk factors have also been identified. Cigarette smoking is shown to be a major risk factor of anxiety disorder onset, while smoking cessation is associated with reduced anxiety, suggesting that smoking interventions would have a significant effect on anxiety disorder onset [110; 111]. Another important risk factor of anxiety disorder onset in longitudinal studies is the occurrence of adverse life events, such as the ending of a relationship or the injury, illness, or death of a loved one [112; 113; 114].

The presence of adverse events at baseline is associated with an increased risk of overall anxiety disorder onset in older adults. In addition to female sex, history of any mood disorder, and cigarette smoking at baseline, lower levels of educational achievement are associated with higher risk of anxiety disorder onset at follow-up. Although previous studies have reported that excessive anxiety may be a result of licit or illicit substance use or abuse, this has not been replicated in more recent analyses [115; 116; 117]. The association between anxiety disorder and increased substance abuse (including prescription medication) observed in prior studies has been interpreted as evidence of self-medication for emotional distress [118; 119; 120]. A 2019 study

assessed the longitudinal association of baseline social anxiety disorder and incident alcohol use disorder at 3- and 10-year follow-up periods in two national samples and did not find evidence of an association between social anxiety and self-medication with alcohol [121].

The prevalence of anxiety disorder is substantially higher in medical versus community settings, and there is a particularly high prevalence of anxiety disorder in individuals with Parkinson disease and among caregivers of older adults [51; 61; 122; 123; 124; 125]. Studies have demonstrated that, in part, the psychological distress (e.g., anxiety and depression) experienced by caregivers is linked to their patients' overall cognitive well-being, patient functional ability, and the reported caregiver burden [126; 127; 128; 129].

TREATMENT

This section will review the available evidence base for the treatment of anxiety disorders. First, preference is given to systematic reviews and network meta-analyses in the general population. However, individual studies are also used in discussion of specific phobia due to a lack of more rigorous research.

PANIC DISORDER

A 2016 network meta-analysis of 54 intervention studies assessed the effectiveness of eight methods of psychological interventions for treating panic disorder with or without agoraphobia [130]. These interventions included [130]:

- Psychoeducation
- Supportive psychotherapy
- Physiological therapies
- Behavior therapy
- Cognitive therapy
- Cognitive behavioral therapy (CBT)
- Third-wave CBT
- Psychodynamic therapies

Researchers found that not one of these treatments was supported as being more efficacious than the others, although any psychological treatment was generally mildly efficacious in comparison with a wait-list control condition [130]. In a subsequent study, the same investigators assessed whether particular components of CBT were associated with better responses to treatment. They reported that face-to-face administration (as compared to self-help) and graded interoceptive exposure to the physiological aspects of the panic response are the most effective features of CBT for treating panic disorder, although it is important to note that the principle of totality applies: the whole of a treatment is more than the sum of its parts [131]. Individual studies addressing treatments for late-life panic disorder have found that both psychological and pharmacological interventions tend to be less efficacious for older adults compared with younger adults [132].

SOCIAL ANXIETY DISORDER

A systematic review and network meta-analysis compared the effectiveness of seven classes of psychological interventions, five classes of pharmacological interventions, and three control groups [133]. Interventions included:

- Promotion of exercise
- Exposure and social skills
- Group CBT
- Individual CBT
- Other psychological therapy (including interpersonal psychotherapy, mindfulness training, and supportive therapy)
- Psychodynamic psychotherapy
- Self-help with or without support

Individual CBT was found to be effective for acute treatment compared with waitlist control groups. Pharmacologic interventions included anticonvulsants, benzodiazepines, monoamine oxidase inhibitors (MAOIs), noradrenergic and

serotonergic antidepressants, selective serotonin reuptake inhibitors (SSRIs), and selective norepinephrine reuptake inhibitors (SNRIs). SSRIs and SNRIs were found to be the most effective class of pharmacological treatment compared with placebo control groups [133].

In this study, the promotion-of-exercise intervention was not found to be effective; however, this was not actually an exercise intervention. A 2020 systematic review and network meta-analysis assessing the efficacy of aerobic, resistance, and mind-body training regimens for treating depression reported that actual exercise interventions elicit high levels of treatment compliance and can be effective in reducing depressive symptoms [134]. Thus, similar treatments may also prove to be efficacious for treating anxiety disorders or subtypes.

GENERALIZED ANXIETY DISORDER

The results of two systematic reviews and meta-analyses suggest that psychological therapy has short-term efficacy for treating GAD [135]. A systematic review and network meta-analysis of 27 randomized, double-blind, placebo-controlled studies compared the relative effectiveness of nine pharmacologic treatments of GAD [136]. Although none of the treatments stood out as being clearly more successful than the others, it was concluded that fluoxetine may be preferred for response and remission and sertraline for treatment tolerance. Sertraline is also the most cost-effective pharmacologic treatment of GAD [137]. A separate systematic review and meta-analysis of 27 clinical trials assessed the effectiveness of psychological and pharmacologic treatments for late-life GAD [41]. In this study, benzodiazepines were found to be mildly efficacious relative to placebo, and psychotherapy was found to be mildly efficacious relative to waitlist control groups. A 2016 meta-analysis also reported that CBT is effective for treating GAD in older adults [138].



According to the National Collaborating Centre for Mental Health, the recommended high-intensity psychological intervention for persons with generalized anxiety disorder is cognitive-behavioral therapy (CBT) or applied relaxation.

(<https://www.nice.org.uk/guidance/cg113>. Last accessed February 17, 2022.)

Level of Evidence: Expert Opinion/Consensus Statement

SPECIFIC PHOBIAS

Exposure therapy is the treatment of choice for specific phobias [139; 140]. This includes in vivo (real-life) and virtual reality exposure to phobic stimuli or situations. Virtual reality exposure therapy was introduced in the 1990s, and although it may have some treatment benefit, it has not been found to have strong efficacy [141]. A one-session exposure therapy treatment for specific phobias was pioneered more than 30 years ago with a suggested duration of two hours and was subsequently used to treat various specific phobia subtypes [142; 143; 144; 145]. More recent studies suggest that one session does not always turn out to be adequate and that multiple sessions are generally more efficacious [140; 146]. However, there may be some cases where the single-session approach is viable.



The National Collaborating Centre for Mental Health recommends against routinely offering computerized CBT to treat specific phobias in adults.

([https://www.nice.org.uk/guidance/cg159/resources/social-anxiety-](https://www.nice.org.uk/guidance/cg159/resources/social-anxiety-disorder-recognition-assessment-and-treatment-pdf-35109639699397)

[disorder-recognition-assessment-and-treatment-pdf-35109639699397](https://www.nice.org.uk/guidance/cg159/resources/social-anxiety-disorder-recognition-assessment-and-treatment-pdf-35109639699397). Last accessed February 17, 2022.)

Level of Evidence: Expert Opinion/Consensus Statement

Pharmacotherapy is not a common treatment for specific phobias. However, studies have sought to supplement exposure therapy using pharmacologic approaches. One such intervention administers cortisol to augment exposure therapy due to its role in interfering with memory for fearful scenarios [147; 148]. Although this treatment shows some efficacy, it does not seem to be particularly advantageous relative to exposure therapy alone. A second form of pharmacologic augmentation for exposure therapy, introduced more than 20 years ago, is the antibiotic D-cycloserine, which is thought to facilitate fear extinction due to its role as an *N*-methyl D-aspartate (NMDA) receptor agonist [149; 150]. D-cycloserine has also been used to augment exposure therapy for social anxiety disorder, with studies suggesting that this antibiotic can produce a marginal benefit for treating specific phobias and social anxiety disorder when combined with exposure therapy [151]. However, while these studies mention that the antibiotic is of a low dosage, they do not mention that this marginal benefit needs to be traded off against the risk of accelerating antibiotic resistance, which is a pressing global public health challenge. Computational studies suggest that increasing administration of low doses of antibiotics (as these studies suggest doing in conjunction with exposure therapy) accelerates resistance [152; 153].

Although the short-term efficacy of exposure therapy for specific phobias is moderately high, it is important to note that specific phobias are prone to high rates of relapse [139; 140; 154; 155; 156; 157]. Accordingly, studies have sought to eliminate conditioned responses to phobic stimuli over multiple contexts to make for a more successful extinction [158; 159; 160; 161; 162].

TREATMENT IMPLICATIONS

Given that anxiety itself is an adaptive trait, anxiety disorders are better seen as poorly regulated defenses than as defects. As decades of lesion studies indicate, a lack of anxiety may also create non-trivial problems for individuals' lives. Low levels of anxiety are associated with higher mortality risk, and those who report greater worries about particular health problems are likely to seek medical care and take preventative or corrective action [39; 103; 104; 105; 106; 107]. If some degree of anxiety is advantageous, then insufficient and excessive anxiety can both be considered maladaptive.

CONCLUSION

Anxiety facilitates the management of potential future hazards. Even though anxiety is effective at reducing danger, excessive anxiety is often a cause of significant distress and impairment, and anxiety disorders are the most prevalent mental disorders among older adults. Female sex and smoking are the strongest risk factors for late-life anxiety disorders, although adverse life events are also an important factor. About one-third of all cases have considerable chronicity, and therefore prevention is important. Interventions should focus on reducing anxiety to a sufficient, but not excessive, degree.

Works Cited

1. Crocq M-A. A history of anxiety: from Hippocrates to DSM. *Dialogues Clinl Neurosci*. 2015;17(3):319-325.
2. Darwin C. *The Expression of Emotion in Man and Animals*. London: John Murray; 1872.
3. Bateson M, Brilot B, Nettle D. Anxiety: an evolutionary approach. *Can J Psychiatry*. 2011;56(12):707-715.
4. Marks IM, Nesse RM. Fear and fitness: an evolutionary analysis of anxiety disorders. *Ethol Sociobiol*. 1994;15(5-6):247-261.
5. Miloyan B, Bulley A, Bandeen-Roche K, Eaton WW, Gonçalves-Bradley DC. Anxiety disorders and all-cause mortality: systematic review and meta-analysis. *Soc Psychiatry Psychiatr Epidemiol*. 2016;51(11):1467-1475.
6. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders* (5th ed). Arlington, VA: American Psychiatric Association; 2013.
7. World Health Organization. ICD-10 Classification of Mental and Behavioral Disorders—Diagnostic Criteria for Research, 11th edition. Available at <https://icd.who.int/en>. Last accessed August 12, 2020.
8. Nesse RM. The smoke detector principle: natural selection and the regulation of defensive responses. *Ann N Y Academy Sci*. 2001;935:75-85.
9. Nesse RM. Natural selection and the regulation of defenses: a signal detection analysis of the smoke detector principle. *Evol Hum Behav*. 2005;26(1):88-105.
10. Mogg K, Bradley BP. A cognitive-motivational analysis of anxiety. *Behav Res Ther*. 1998;36(9):809-848.
11. Moniz E. Prefrontal leucotomy in the treatment of mental disorders 1937. *Am J Psychiatry*. 1994;151(6 Suppl):236-239.
12. Steele GDF. Persistent anxiety and tachycardia successfully treated by prefrontal leucotomy. *Br Med J*. 1951;2(4723):84-86.
13. Koenigs M, Huey ED, Calamia M, Raymond V, Tranel D, Grafman J. Distinct regions of prefrontal cortex mediate resistance and vulnerability to depression. *J Neurosci*. 2008;28(47):12341-12348.
14. Koenigs M, Huey ED, Raymond V, et al. Focal brain damage protects against post-traumatic stress disorder in combat veterans. *Nat Neurosci*. 2008;11(2):232-237.
15. Koenigs M, Grafman J. Posttraumatic stress disorder: the role of medial prefrontal cortex and amygdala. *Neuroscientist*. 2009;15(5):540-548.
16. Myers-Schulz B, Koenigs M. Functional anatomy of ventromedial prefrontal cortex: implications for mood and anxiety disorders. *Mol Psychiatry*. 2012;17:132-141.
17. Bechara A, Damasio H, Tranel D, Damasio AR. Deciding advantageously before knowing the advantageous strategy. *Science*. 1997;275(5304):1293-1295.
18. Damasio AR, Tranel D, Damasio H. Individuals with sociopathic behavior caused by frontal damage fail to respond autonomically to social stimuli. *Behav Brain Res*. 1990;41(2):81-94.
19. Motzkin JC, Philippi CL, Wolf RC, Baskaya MK, Koenigs M. Ventromedial prefrontal cortex lesions alter neural and physiological correlates of anticipation. *J Neurosci*. 2014;34(31):10430-10437.
20. Philippi CL, Koenigs M. The neuropsychology of self-reflection in psychiatric illness. *J Psychiatr Res*. 2014;54:55-63.
21. Schneider B, Koenigs M. Human lesion studies of ventromedial prefrontal cortex. *Neuropsychologia*. 2017;107:84-93.
22. Feinstein JS, Adolphs R, Damasio AR, Tranel D. The human amygdala and the induction and experience of fear. *Curr Biol*. 2011;21(1):34-38.
23. Bovasso G, Eaton W. Types of panic attacks and their association with psychiatric disorder and physical illness. *Compr Psychiatry*. 1999;4(6):469-477.
24. Briggs AC, Stretch DD, Brandon S. Subtyping of panic disorder by symptom profile. *Br J Psychiatry*. 1993;163:201-209.
25. Roberson-Nay R, Kendler KS. Panic disorder and its subtypes: a comprehensive analysis of panic symptom heterogeneity using epidemiological and treatment seeking samples. *Psychol Med*. 2011;41(11):2411-2421.
26. Deer TM, Calamari JE. Panic symptomatology and anxiety sensitivity in older adults. *Journal of Behavior Therapy & Experimental Psychiatry*. 1998;29(4):303-316.
27. Keyl PM, Eaton WW. Risk factors for the onset of panic disorder and other panic attacks in a prospective, population-based study. *Am J Epidemiol*. 1990;131(2):301-311.
28. McCabe L, Cairney J, Veldhuizen S, Herrmann N, Streiner DL. Prevalence and correlates of agoraphobia in older adults. *Am J Geriatr Psychiatry*. 2006;14(6):515-522.
29. Sheikh JI, Swales PJ, Carlson EB, Lindley SE. Aging and panic disorder: phenomenology, comorbidity, and risk factors. *Am J Geriatr Psychiatry*. 2004;12(1):102-109.
30. Wittchen HU, Reed V, Kessler RC. The relationship of agoraphobia and panic in a community sample of adolescents and young adults. *Arch Gen Psychiatry*. 1998;55(11):1017-1024.
31. National Institute on Alcohol Abuse and Alcoholism. National Epidemiological Survey on Alcohol and Related Conditions. Available at <https://www.niaaa.nih.gov/research/nesarc-iii>. Last accessed February 8, 2022.

32. Depla MFIA, ten Have ML, van Balkom AJLM, de Graaf R. Specific fears and phobias in the general population: results from the Netherlands Mental Health Survey and Incidence Study (NEMESIS). *Social Psychiatry & Psychiatric Epidemiology*. 2008;43(3):200-208.
33. Magee WJ, Eaton WW, Wittchen HU, McGonagle KA, Kessler RC. Agoraphobia, simple phobia, and social phobia in the National Comorbidity Survey. *Archives of General Psychiatry*. 1996;53(2):159-168.
34. Stinson FS, Dawson DA, Chou SP, et al. The epidemiology of DSM-IV specific phobia in the USA: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Psychol Med*. 2007;37(7):1047-1059.
35. Grenier S, Schuurmans J, Goldfarb M, et al. The epidemiology of specific phobia and subthreshold fear subtypes in a community-based sample of older adults. *Depress Anxiety*. 2011;28(6):456-463.
36. Miloyan B, Eaton WW. Blood-injection-injury phobia in older adults. *Int Psychogeriatr*. 2016;28(6):897-902.
37. Gretarsdottir E, Woodruff-Borden J, Meeks S, Depp CA. Social anxiety in older adults: phenomenology, prevalence, and measurement. *Behav Res Ther*. 2004;42(4):459-475.
38. Miloyan B, Bulley A, Pachana NA, Byrne GJ. Social phobia symptoms across the adult lifespan. *J Affect Disord*. 2014;168(15):86-90.
39. Watkins ER. Constructive and unconstructive repetitive thought. *Psychol Bull*. 2008;134(2):163-206.
40. Basevitz P, Pushkar D, Chaikelson J, Conway M, Dalton C. Age-related differences in worry and related processes. *Int J Aging Hum Dev*. 2008;66(4):283-305.
41. Gonçalves DC, Byrne GJ. Who worries most? Worry prevalence and patterns across the lifespan. *Int J Geriatr Psychiatry*. 2013;28(1):41-49.
42. Gould CE, Edelstein BA. Worry, emotional control, and anxiety control in older and young adults. *J Anxiety Disord*. 2010;24(7):759-766.
43. Hunt S, Wisocki P, Yanko J. Worry and use of coping strategies among older and younger adults. *J Anxiety Disord*. 2003;17(5):547-560.
44. Lindsay J, Baillon S, Brugha T, et al. Worry content across the lifespan: an analysis of 16- to 74-year-old participants in the British National Survey of Psychiatric Morbidity 2000. *Psychol Med*. 2006;36(11):1625-1633.
45. Miloyan B, Pachana NA. Clinical significance of worry and physical symptoms in late-life generalized anxiety disorder. *Int J Geriatr Psychiatry*. 2015;30(12):1186-1194.
46. Powers CB, Wisocki PA, Whitbourne SK. Age differences and correlates of worrying in young and elderly adults. *Gerontologist*. 1992;32(1):82-88.
47. Petku, A, Merz C, Wetherell JL. Anxiety disorders in older adulthood. In: Emmelkamp P, Ehring T (eds). *The Wiley Handbook of Anxiety Disorders*. Malden, MA: Wiley-Blackwell; 2014: 599-611.
48. Wetherell JL. Worry in older adults. In: Davey GC, Wells A (eds). *Worry and Its Psychological Disorders: Theory, Assessment and Treatment*. Chichester: John Wiley & Sons; 2006: 70-79.
49. Anthony-Bergstone CR, Zarit SH, Gatz M. Symptoms of psychological distress among caregivers of dementia patients. *Psychol Aging*. 1988;3(3):245-248.
50. Lim WS, Cheah WK, Ali N, et al. Worry about performance: a unique dimension of caregiver burden. *Int Psychogeriatr*. 2014;26(4):677-696.
51. Razani J, Corona R, Quilici J, et al. The effects of declining functional abilities in dementia patients and increases in psychological distress on caregiver burden over a one-year period. *Clin Gerontol*. 2014;37(3):235-252.
52. Litwin H, Meir A. Financial worry among older people: who worries and why? *J Aging Stud*. 2013;27(2):113-120.
53. Diefenbach GJ, Stanley MA, Beck JG. Worry content reported by older adults with and without generalized anxiety disorder. *Aging Ment Health*. 2001;5(3):269-274.
54. Miloyan B, Byrne GJ, Pachana NA. Threshold and subthreshold generalized anxiety disorder in later life. *Am J Geriatr Psychiatry*. 2015;23(6):633-641.
55. Wolitzky-Taylor KB, Castriotta N, Lenze EJ, Stanley MA, Craske M.G., Anxiety disorders in older adults: a comprehensive review. *Depress Anxiety*. 2010;27(2):190-211.
56. Robins LN, Helzer JE, Croughan J, Ratcliff KS. National Institute of Mental Health Diagnostic Interview Schedule: its history, characteristics, and validity. *Arch Gen Psychiatry*. 1981;38(4):381-389.
57. Kessler RC, Üstün TB. The World Mental Health (WMH) Survey Initiative Version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). *Int J Methods Psychiatr Res*. 2004;13(2):93-121.
58. Di Nardo PA, O'Brien GT, Barlow DH, Waddell MT, Blanchard EB. Reliability of DSM-III anxiety disorder categories using a new structured interview. *Arch Gen Psychiatry*. 1983;40(10):1070-1074.
59. Williams JB, Gibbon M, First MB, et al. The structured clinical interview for DSM-III-R (SCID). II. Multisite test-retest reliability. *Arch Gen Psychiatry*. 1992;49(8):630-636.

60. Wing JK, Babor T, Brugha T, et al. SCAN: Schedules for Clinical Assessment in Neuropsychiatry. *Arch Gen Psychiatry*. 1990;47(6):589-593.
61. Kroenke K, Spitzer RL, Williams JBW, Monahan PO, Löwe B. Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. *Ann Intern Med*. 2007;146(5):317-325.
62. Spitzer RL, Kroenke K, Williams JBW, Löwe BA. Brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med*. 2006;166(10):1092-1097.
63. Plummer F, Manea L, Trepel D, McMillan D. Screening for anxiety disorders with the GAD-7 and GAD-2: a systematic review and diagnostic meta-analysis. *Gen Hosp Psychiatry*. 2016;39:24-31.
64. Shear MK, Brown TA, Barlow DH, et al. Multicenter collaborative Panic Disorder Severity Scale. *Am J Psychiatry*. 1997;154(11):1571-1575.
65. Shear MK, Rucci P, Williams J, et al. Reliability and validity of the Panic Disorder Severity Scale: replication and extension. *J Psychiatr Res*. 2001;35(5):293-296.
66. Connor KM, Davidson JRT, Churchill LE, Sherwood A, Foa E, Weisler RH. Psychometric properties of the Social Phobia Inventory (SPIN): new self-rating scale. *Br J Psychiatry*. 2000;176:379-386.
67. Connor KM, Kobak KA, Churchill LE, Katzelnick D, Davidson JRT. Mini-SPIN: a brief screening assessment for generalized social anxiety disorder. *Depress Anxiety*. 2001;14(2):137-140.
68. Seeley-Wait E, Abbott MJ, Rapee RM. Psychometric properties of the Mini-Social Phobia Inventory. *J Clin Psychiatry*. 2009;11(5):231-236.
69. Norman SB, Cissell SH, Means-Christensen AJ, Stein MB. Development and validation of an Overall Anxiety Sensitivity and Impairment Scale (OASIS). *Depress Anxiety*. 2006;23(4):245-249.
70. Norman SB, Campbell-Sills L, Hitchcock CA, et al. Psychometrics of a brief measure of anxiety to detect severity and impairment: the Overall Anxiety Severity and Impairment Scale. *J Psychiatr Res*. 2011;45(2):262-268.
71. Bragdon LB, Diefenbach GJ, Hannan S, Tolin DF. Psychometric properties of the Overall Anxiety Severity and Impairment Scale (OASIS) among psychiatric outpatients. *J Affect Disord*. 2016;201:112-115.
72. Byrne GJ, Pachana NA, Gonçalves DC, Arnold E, King R, Khoo SK. Psychometric properties and health correlates of the Geriatric Anxiety Inventory in Australian community-residing older women. *Aging Ment Health*. 2010;14(3):247-254.
73. Pachana NA, Byrne GJ, Siddle H, Koloski N, Harley E, Arnold E. Development and validation of the Geriatric Anxiety Inventory. *Int Psychogeriatr*. 2007;19(1):103-114.
74. Johnco C, Knight A, Tadic D, Wuthrich VM. Psychometric properties of the Geriatric Anxiety Inventory (GAI) and its short-form (GAI-SF) in a clinical and non-clinical sample of older adults. *Int Psychogeriatr*. 2015;27(7):1089-1097.
75. Boddice G, Pachana NA, Byrne GJ. The clinical utility of the geriatric anxiety inventory in older adults with cognitive impairment. *Nurs Older People*. 2008;20(8):36-39.
76. Matheson SF, Byrne GJ, Dissanayaka NN, et al. Validity and reliability of the Geriatric Anxiety Inventory in Parkinson's disease. *Australas J Ageing*. 2010;31(1):13-16.
77. Byrne GJ, Pachana NA. Development and validation of a short form of the Geriatric Anxiety Inventory: the GAI-SF. *Int Psychogeriatr*. 2011;23(1):125-131.
78. Segal DL, June A, Payne M, Coolidge FL, Yochim B. Development and initial validation of a self-report assessment tool for anxiety among older adults: the Geriatric Anxiety Scale. *J Anxiety Disord*. 2010;24:709-714.
79. Mueller AE, Segal DL, Gavett B, et al. Geriatric Anxiety Scale: item response theory analysis, differential item functioning, and creation of a ten-item short form (GAS-10). *Int Psychogeriatr*. 2015;27(7):1099-1111.
80. Guzmán-Vélez E, Feinstein JS, Tranel D. Feelings without memory in Alzheimer disease. *Cogn Behav Neurol*. 2014;27(3):117-129.
81. McDade-Montez EA, Watson D, O'Hara MW, Denburg NL. The effect of symptom visibility on informant reporting. *Psychology and Aging*. 2008;23(4):940-946.
82. Streiner DL, Patten SB, Anthony J, Cairney J. Has "lifetime prevalence" reached the end of its life? An examination of the concept. *Int J Methods Psychiatr Res*. 2009;18(4):221-228.
83. Schacter DL, Gaesser B, Addis DR. Remembering the past and imagining the future in the elderly. *Gerontology*. 2014;59(2):143-151.
84. Reynolds K, Pietrzak RH, El-Gabalawy R, Mackenzie CS, Sareen J. Prevalence of psychiatric disorders in U.S. older adults: findings from a nationally representative survey. *World Psychiatry*. 2015;14(1):74-81.
85. Asnaani A, Richey JA, Dimaite R, Hinton DE, Hofmann SG. A Cross-ethnic comparison of lifetime prevalence rates of anxiety disorders. *J Nerv Ment Dis*. 2010;198(8):551-555.
86. Grant B, Goldstein RB, Chou SP, et al. Sociodemographic and psychopathologic predictors of first incidence of DSM-IV substance use, mood and anxiety disorders: results from the Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions. *Mol Psychiatry*. 2009;14(11):1051-1066.

87. Beesdo K, Pine DS, Lieb R, Wittchen H-U. Incidence and risk patterns of anxiety and depressive disorders and categorization of generalized anxiety disorder. *Arch Gen Psychiatry*. 2010;67(1):47-57.
88. Bijl RV, De Graaf R, Ravelli A, Smit F, Vollebergh WAM, Netherlands Mental Health Survey and Incidence Study. Gender and age-specific first incidence of DSM-III-R psychiatric disorders in the general population. Results from the Netherlands Mental Health Survey and Incidence Study (NEMESIS). *Soc Psychiatry Psychiatr Epidemiol*. 2002;37(8):372-379.
89. Eaton WW, Alexandre P, Kessler RC, et al. The population dynamics of mental disorders. In: Eaton WW (ed). *Public Mental Health*. New York, NY: Oxford University Press; 2014.
90. Grant B, Hasin DS, Blanco C, et al. The epidemiology of social anxiety disorder in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *J Clin Psychiatry*. 2005;66(11):1351-1361.
91. Grant B, Hasin DS, Stinson FS. Prevalence, correlates, co-morbidity, and comparative disability of DSM-IV generalized anxiety disorder in the USA: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Psychol Med*. 2005;35(12) :1747-1759.
92. Almeida OP, Draper B, Pirkis J, et al. Anxiety, depression, and comorbid anxiety and depression: risk factors and outcome over two years. *Int Psychogeriatr*. 2012;24(10):1622-1632.
93. Beekman AT, de Beurs E, Van Balkom AJ, Deeg DJ, Van Dyck R, van Tilburg W. Anxiety and depression in later life: co-occurrence and communality of risk factors. *Am J Psychiatry*. 2000;157(1):89-95.
94. Kessler RC, Chiu WT, Jin R, Ruscio AM, Shear K, Walters EE. The epidemiology of panic attacks, panic disorder, and agoraphobia in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2006;63(4):415-424.
95. Wardenaar KJ, Huang Y, Wojtyniak B, de Jonge P. Comorbidity: the cross-national structure of mental disorders. In: Scott KM, de Jonge P, Stein DJ, Kessler RC (eds). *Mental Disorders Around the World: Facts and Figures from the WHO World Mental Health Surveys*. Cambridge: Cambridge University Press; 2018: 297-313.
96. Sareen J, Cox BJ, Afifi TO, et al. Anxiety disorders and risk for suicidal ideation and suicide attempts: a population-based longitudinal study of adults. *Arch Gen Psychiatry*. 2005;62(11):1249-1257.
97. Wilgoss TG, Yohannes AM. Anxiety disorders in patients with COPD: a systematic review. *Respir Care*. 2013;58(5):858-866.
98. Bienvenu O J, Eaton WW. The epidemiology of blood-injection-injury phobia. *Psychol Med*. 1998;28(5):1129-1136.
99. Witthauer C, Ajdacic-Gross V, Meyer AH, et al. Associations of specific phobia and its subtypes with physical diseases: an adult community study. *BMC Psychiatry*. 2016;16.
100. Sigström R, Östling S, Karlsson B, Waern M, Gustafson D, Skoog I. A population-based study on phobic fears and DSM-IV specific phobia in 70-year olds. *J Anxiety Disord*. 2011;25(1):148-153.
101. Sareen J, Cox BJ, Clara I, Asmundson GJG. The relationship between anxiety disorders and physical disorders in the U.S. National Comorbidity Survey. *Depress Anxiety*. 2005;21(4):193-202.
102. Thibodeau MA, Welch PG, Sareen J, Asmundson GJG. Anxiety disorders are independently associated with suicide ideation and attempts: propensity score matching in two epidemiological samples. *Depress Anxiety*. 2013;30(10):947-954.
103. Mykletun A, Bjerkeset O, Overland S, Prince M, Dewey M, Stewart R. Levels of anxiety and depression as predictors of mortality: the HUNT study. *Br J Psychiatry*. 2019;195(2):118-125.
104. Lee WE, Wadsworth MEJ, Hotopf M. The protective role of trait anxiety: a longitudinal cohort study. *Psychol Med*. 2006;36(3):345-351.
105. Hay JL, McCaul KD, Magnan RE. Does worry about breast cancer predict screening behaviors? A meta-analysis of the prospective evidence. *Preventive Medicine*. 2006;42(6):401-408.
106. Chapman GB, Coups EJ. Emotions and preventive health behavior: worry, regret, and influenza vaccination. *Health Psychology*. 2006;25(1):82-90.
107. Dijkstra A, Brosschot J. Worry about health in smoking behaviour change. *Behaviour Research and Therapy*. 2003;41(9):1081-1092.
108. Byers AL, Yaffe K, Covinsky KE, Friedman MB, Bruce ML. High occurrence of mood and anxiety disorders among older adults: the National Comorbidity Survey-Replication. *Arch Gen Psychiatry*. 2010;67(5):489-496.
109. Prévaille M, Boyer R, Grenier S, et al. The epidemiology of psychiatric disorders in Quebec's older adult population. *Can J Psychiatry*. 2008;53(12):822-832.
110. Mojtabai R, Crum RM. Cigarette smoking and onset of mood and anxiety disorders. *Am J Public Health*. 2013;103(9):1656-1665.
111. Taylor G, McNeill A, Girling A, Farley A, Lindson-Hawley N, Aveyard P. Change in mental health after smoking cessation: systematic review and meta-analysis. *BMJ*. 2014;348:g1151.
112. Francis JL, Moitra E, Dyck I, Keller MB. The impact of stressful life events on relapse of generalized anxiety disorder. *Depress Anxiety*. 2012;29(5):386-391.
113. Keyes KM, Pratt C, Galea S, McLaughlin KA, Koenen KC, Shear MK. The burden of loss: unexpected death of a loved one and psychiatric disorders across the life course in a national study. *Am J Psychiatry*. 2014;171(8):864-871.
114. Taher D, Mahmud N, Amin R. The effect of stressful life events on generalized anxiety disorder. *European Psychiatry*. 2015;30(Suppl 1):543.

115. Fenton MC, Keyes KM, Martins SS, Hasin DS. The role of a prescription in anxiety medication use, abuse, and dependence. *Am J Psychiatry*. 2010;167(10):1247-1253.
116. Martins SS, Fenton MC, Keyes KM, Blanco C, Zhu H, Storr CL. Mood/anxiety disorders and their association with non-medical prescription opioid use and prescription opioid-use disorder: longitudinal evidence from the National Epidemiologic Study on Alcohol and Related Conditions. *Psychol Med*. 2012;42(6):1261-1272.
117. Melchior M, Prokofyeva E, Younès N, Surkan PJ, Martins SS. Treatment for illegal drug use disorders: the role of comorbid mood and anxiety disorders. *BMC Psychiatry*. 2014;14:89.
118. Martins SS, Gorelick DA. Conditional substance abuse and dependence by diagnosis of mood or anxiety disorder or schizophrenia in the U.S. population. *Drug Alcohol Depend*. 2011;119(1-2):28-36.
119. Bulley A, Miloyan B, Brilot B, Gullo MJ, Suddendorf T. An evolutionary perspective on the co-occurrence of social anxiety. *J Affect Disord*. 2016;196:62-70.
120. Khantzian EJ. The self-medication hypothesis of addictive disorders: focus on heroin and cocaine dependence. *Am J Psychiatry*. 1985;142(11):1259-1264.
121. Miloyan B, Van Doorn G. Longitudinal association between social anxiety disorder and incident alcohol use disorder: results from two national samples of US adults. *Soc Psychiatry Psychiatr Epidemiol*. 2019;54(4):469-475.
122. Dissanayaka NN, Sellbach A, Matheson S, O'Sullivan JD. Anxiety disorders in Parkinson's disease: prevalence and risk factors. *Movement Disorders*. 2010;25(7):838-845.
123. Leentjens AF, Dujardin K, Marsh L, Martinez-Martin P, Richard IH, Starkstein SE. Symptomatology and markers of anxiety disorders in Parkinson's disease: a cross-sectional study. *Mov Disord*. 2011;26(3):484-492.
124. Pontone GM, Williams JR, Anderson KE, et al. Prevalence of anxiety disorders and anxiety subtypes in patients with Parkinson's disease. *Move Disord*. 2009;24(9):1333-1338.
125. Stenberg U, Ruland CM, Miaskowski C. Review of the literature on the effects of caring for a patient with cancer. *Psychooncology*. 2010;19(10):1013-1025.
126. Berger G, Bernhardt T, Weimer E, Peters J, Kratzsch T, Frolich L. Longitudinal study on the relationship between symptomatology of dementia and levels of subjective burden in depression among family caregivers in memory clinic patients. *J Geriatr Psychiatry Neurol*. 2005;18(3):119-128.
127. Hirschman KB, Xie SX, Feudtner C, Karlawish JHT. How does an Alzheimer's disease patient's role in medical decision-making change over time? *J Geriatr Psychiatry Neurol*. 2004;17(2):55-60.
128. Razani J, Kakos B, Orita-Barbalace C, et al. Predicting caregiver burden from daily functional abilities of patients with mild dementia. *J Am Geriatr Soc*. 2007;55(9):1415-1420.
129. Epstein-Lubow G, Davis JD, Miller IW, Tremont G. Persisting burden predicts depressive symptoms in dementia caregivers. *J Geriatr Psychiatry Neurol*. 2008;21(3):198-203.
130. Pompoli A, Furukawa TA, Imai H, Tajika A, Efthimiou O, Salanti G. Psychological therapies for panic disorder with or without agoraphobia in adults: a network meta-analysis. *Cochrane Database Syst Rev*. 2016;4(4):CD011004.
131. Pompoli A, Furukawa TA, Efthimiou O, Imai H, Tajika A, Salanti G. Dismantling cognitive-behaviour therapy for panic disorder: a systematic review and component network meta-analysis. *Psychol Med*. 2018;48(12):1945-1953.
132. Wetherell J, Petkus AJ, Throp SR, et al. Age differences in treatment response to a collaborative care intervention for anxiety disorders. *Br J Psychiatry*. 2013;203(1):65-72.
133. Mayo-Wilson E, Dias S, Mavranouzouli I, et al. Psychological and pharmacological interventions for social anxiety disorder in adults: a systematic review and network meta-analysis. *Lancet Psychiatry*. 2014;1(5):368-376.
134. Miller KJ, Gonçalves-Bradley DC, Areerob P, Hennessy D, Mesagno C, Grace F. Comparative effectiveness of three exercise types to treat clinical depression in older adults: a systematic review and network meta-analysis of randomised controlled trials. *Ageing Res Rev*. 2020;58:100999.
135. Cuijpers P, Sijbrandij M, Koole S, Huibers M, Berking M, Andersson G. Psychological treatment of generalized anxiety disorder: a meta-analysis. *Clin Psychol Rev*. 2014;34(2):130-140.
136. Baldwin D, Woods R, Lawson R, Taylor D. Efficacy of drug treatments for generalized anxiety disorder: systematic review and meta-analysis. *BMJ*. 2011;342:d1199.
137. Mavranouzouli I, Meader N, Cape J, Kendall T. The cost effectiveness of pharmacological treatments for generalized anxiety disorder. *PharmacoEconomics*. 2013;31(4):317-333.
138. Hall J, Kellett S, Berrios R, Bains MK, Scott S. Efficacy of cognitive behavioral therapy for generalized anxiety disorder in older adults: systematic review, meta-analysis, and meta-regression. *Am J Geriatr Psychiatry*. 2016;24(11):1063-1073.
139. Choy Y, Fyer AJ, Lipsitz JD. Treatment of specific phobia in adults. *Clin Psychol Rev*. 2007;27(3):266-286.
140. Wolitzky-Taylor KB, Horowitz JD, Powers MB, Telch MJ. Psychological approaches in the treatment of specific phobias: a meta-analysis. *Clin Psychol Rev*. 2008;28(6):1021-1037.
141. Rothbaum BO, Hodges LF, Kooper R, Opdyke D, Williford JS, North M. Effectiveness of computer-generated (virtual reality) graded exposure in the treatment of acrophobia. *Am J Psychiatry*. 1995;152(4):626-628.

142. Öst LG. One-session treatment for specific phobias. *Behav Res Ther.* 1989;27(1):1-7.
143. Öst LG, Brandberg M, Alm T. One versus five sessions of exposure in the treatment of flying phobia. *Behav Res Ther.* 1997;35(11):987-996.
144. Öst LG. One-session treatments for a case of multiple simple phobias. *Scandinavian Journal of Behaviour Therapy.* 1987;16(4):175-184.
145. Öst LG, Hellström K, Kåver A. One versus five sessions of exposure in the treatment of injection phobia. *Behav Ther.* 1992;23(2):263-281.
146. Abramowitz JS. The practice of exposure therapy: relevance of cognitive-behavioral theory and extinction theory. *Behav Ther.* 2013;44(4):548-558.
147. de Quervain DJF, Bentz D, Michael T, Bolt OC, et al. Glucocorticoids enhance extinction-based psychotherapy. *Proc Natl Acad Sci USA.* 2011;108(16):6621-6625.
148. Soravia LM, Heinrichs M, Winzeler L, et al. Glucocorticoids enhance in vivo exposure-based therapy of spider phobia. *Depress Anxiety.* 2014;31(5):429-435.
149. Davis M. Role of NMDA receptors and MAP kinase in the amygdala in extinction of fear: clinical implications for exposure therapy. *Eur J Neurosci.* 2002;16(3):395-398.
150. Ressler KJ, Rothbaum BO, Tannenbaum L, et al. Cognitive enhancers as adjuncts to psychotherapy: use of D-cycloserine in phobic individuals to facilitate extinction of fear. *Arch Gen Psychiatry.* 2004;61(11):1136-1144.
151. Mataix-Cols D, Fernández de la Cruz L, Monzani B, et al. D-cycloserine augmentation of exposure-based cognitive behavior therapy for anxiety, obsessive-compulsive, and posttraumatic stress disorders: a systematic review and meta-analysis of individual participant data. *JAMA Psychiatry.* 2017;74(5):501-510.
152. Opatowski L, Mandel J, Varon E, Boëlle P-Y, Temime L, Guillemot D. Antibiotic dose impact on resistance selection in the community: a mathematical model of beta-lactams of streptococcus pneumoniae dynamics. *Antimicrob Agents Chemother.* 2010;54(6):2330-2337.
153. Roberts JA, Druger P, Paterson DL, Lipman J. Antibiotic resistance: what's dosing got to do with it? *Critical Care Medicine.* 2008;36:2433-2440.
154. Bouton ME. Context, ambiguity, and unlearning: sources of relapse after behavioral extinction. *Biol Psychiatry.* 2002;52(10):976-986.
155. Lipsitz JD, Mannuzza S, Klein DF, Ross DC, Fyer AJ. Specific phobia 10–16 years after treatment. *Depression and Anxiety.* 1999;10:105-111.
156. Rodriguez BI, Craske MG, Mineka S, Hladek D. Context-specificity of relapse: effects of therapist and environmental context on return of fear. *Behav Res Ther.* 1999;37(9):845-862.
157. Vervliet B, Craske MG, Hermans D. Fear extinction and relapse: state of the art. *Ann Rev Clin Psychol.* 2013;9:215-248.
158. Bandarian-Balooch, S, Neumann DL, Boschen MJ. Exposure treatment in multiple contexts attenuates return of fear via renewal in high spider fearful individuals. *J Behav Ther Exp Psychiatry.* 2015;47:138-144.
159. Dunsmoor JE, Ahs F, Zielinski DJ, LaBar KS. Extinction in multiple virtual reality contexts diminishes fear reinstatement in humans. *Neurobiol Learn Mem.* 2014;113:157-164.
160. Shiban Y, Pauli P, Mühlberger A. Effect of multiple context exposure on renewal in spider phobia. *Behav Res Ther.* 2013;51(2):68-74.
161. Shiban Y, Schelhorn I, Pauli P, Mühlberger A. Effect of combined multiple contexts and multiple stimuli exposure in spider phobia: a randomized clinical trial in virtual reality. *Behav Res Ther.* 2015;71:45-53.
162. Vansteenwegen D, Vervliet B, Iberico C, Baeyens F, Van den Bergh O, Hermans D. The repeated confrontation with videotapes of spiders in multiple contexts attenuates renewal of fear in spider-anxious students. *Behav Res Ther.* 2007;45(6):1169-1179.

Evidence-Based Practice Recommendations Citations

- National Collaborating Centre for Mental Health. *Social Anxiety Disorder: Recognition, Assessment and Treatment.* London: National Institute for Health and Care Excellence; 2013. Available at <https://www.nice.org.uk/guidance/cg159/resources/social-anxiety-disorder-recognition-assessment-and-treatment-pdf-35109639699397>. Last accessed February 17, 2022.
- National Collaborating Centre for Mental Health, National Collaborating Centre for Primary Care. *Generalised Anxiety Disorder and Panic Disorder in Adults: Management.* London: National Institute for Health and Clinical Excellence; 2019. Available at <https://www.nice.org.uk/guidance/cg113>. Last accessed February 17, 2022.