



Adjustment to Cancer: Anxiety and Distress (PDQ®)—Health Professional Version

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Overview

Studies examining the prevalence of mental disorders in cancer patients [1,2] show that most cancer patients do not meet the diagnostic criteria for any specific mental disorder; however, many do experience a variety of difficult emotional responses.[3]

Psychosocial distress exists on a continuum (refer to the [figure](#) below) ranging from normal adjustment issues through the adjustment disorders of the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5);[4] to a level close to, but below, the threshold (i.e., meets some diagnostic criteria but not all) of diagnosable mental disorders; to syndromes that meet the full diagnostic criteria for a mental disorder (e.g., major depressive disorder). This summary focuses primarily on the less severe end of this continuum: the normal adjustment issues, psychosocial distress,[5] the adjustment disorders, and cancer-related anxiety. (Refer to the PDQ summaries on [Depression](#) and [Cancer-Related Post-traumatic Stress](#) for more information.)

Anxiety is often manifested at various times during cancer screening, diagnosis, treatment, or recurrence. It can sometimes affect a person's behavior regarding his or her health, contributing to a delay in or neglect of measures that might prevent cancer.[6-8] For example, when women with high levels of anxiety learn that they have a genetically higher risk of developing breast cancer than they had previously believed, they might perform breast self-examination less frequently.[9]

For patients undergoing cancer treatment, anxiety can also heighten the expectancy of pain,[10-12] other symptoms of distress, and sleep disturbances, and it can be a major factor in anticipatory nausea and vomiting. Regardless of its severity, anxiety can substantially interfere with the quality of life of cancer patients and their families, and should be evaluated and treated.[13-15]

In this summary, unless otherwise stated, evidence and practice issues as they relate to adults are discussed. The evidence and application to practice related to children may differ significantly from information related to adults. When specific information about the care of children is available, it is summarized under its own heading.

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Definitions

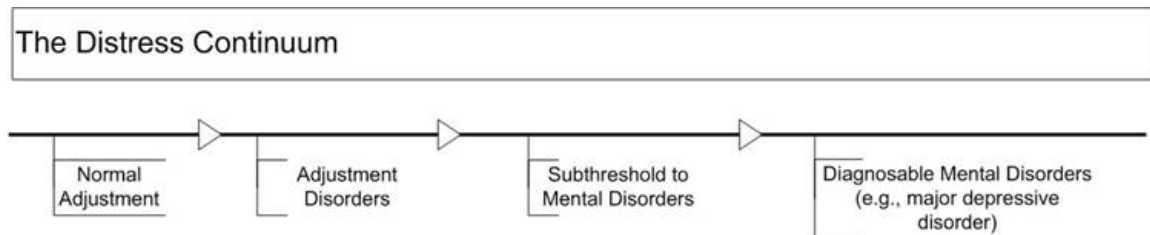
To effectively match patient needs with treatment interventions, health care professionals must be able to distinguish the periodic difficulties that characterize normal adjustment from more-serious mental disorders. To assist in this evaluation, health care professionals need to understand the distinctions among a variety of related concepts, as defined below.

Normal adjustment: Adjustment or psychosocial adaptation to cancer has been defined as an ongoing process in which the individual patient tries to manage emotional distress, solve specific cancer-related problems, and gain mastery of or control over cancer-related life events.[1-3] Adjustment to cancer is not a unitary, single event but rather a series of ongoing coping responses to the multiple tasks associated with living with cancer. (Refer to the [Normal Adjustment](#) section of this summary for more information.)

Psychosocial distress: Distress in cancer has been defined as “a multifactorial unpleasant experience of a psychological (i.e., cognitive, behavioral, emotional), social, spiritual, and/or physical nature that may interfere with the ability to cope effectively with cancer, its physical symptoms, and its treatment. Distress extends along a continuum, ranging from common normal feelings of vulnerability, sadness, and fears to problems that can become disabling, such as depression, anxiety, panic, social isolation, and existential and spiritual crisis.”[4,5] (Refer to the [Psychosocial Distress](#) section of this summary for more information.)

Adjustment disorders: The adjustment disorders, a diagnostic category of the fifth edition of the American Psychiatric Association’s *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5),[6] are characterized by the presence of clinically significant emotional or behavioral symptoms that result in marked distress or significant impairment in social, occupational, or other important areas of functioning. The symptoms occur in response to an identifiable psychosocial stressor (e.g., cancer diagnosis); are less severe than in diagnosable mental disorders such as major depressive disorder or generalized anxiety disorder; and do not represent normal bereavement. (Refer to the [Adjustment Disorders](#) section of this summary for more information.)

Anxiety disorders: Anxiety disorders are a group of mental disorders whose common symptoms include excessive anxiety, worry, fear, apprehension, and/or dread. Although some anxiety can be adaptive—particularly in response to stressors such as cancer—anxiety disorders are excessive, unwarranted, often illogical fears, worry, and dread. The DSM-5 includes generalized anxiety disorder, panic disorder, agoraphobia, social anxiety disorder, specific phobia, obsessive-compulsive disorder, and post-traumatic stress disorder as types of anxiety disorders.[6] (Refer to the [Anxiety Disorders: Description and Etiology](#) section of this summary for more information.)



The distress continuum. Psychosocial distress exists on a continuum that ranges from normal adjustment issues to syndromes that meet the full diagnostic criteria for a mental disorder.

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Risk Factors: Prevalence and Predictors of Distress

A few studies have investigated the prevalence of distress as measured by the National Comprehensive Cancer Network Distress Thermometer (DT) or other screening instruments, such as the Brief Symptom Inventory (BSI).[1-6] Prevalence rates in patients with cancer range from 22% to 58%.[7]

Pooled results from multiple studies suggest that approximately 40% of cancer patients report significant distress.[7] Patients with lung, pancreatic, and brain cancers seem more likely to report distress, but in general, the type of cancer is only modestly associated with distress. Across different cancer types, stronger predictors of distress include disability; poorer quality of life; and ongoing, unmet psychosocial needs.[7]

In regard to prevalence of distress along the clinical course, one study of 236 women newly diagnosed with breast cancer (awaiting their initial consultation with a surgical oncologist) found that 41% reported distress scores higher than 5 on the DT. In this same group of women, 11% reported symptoms suggestive of major depression, and 10% reported symptoms of post-traumatic stress.[8]

Regarding predictors of distress, in a large sample (N = 380) of patients with mixed cancer diagnoses, those reporting a score of 4 or higher on the DT were more likely to be women; to have poorer functional performance (self-reported Karnofsky Performance Scale); and to have reported (on a problem checklist that accompanies the DT) problems with housing, dealing with children, dealing with partner, depression, fears, nervousness, sadness, worry, and 14 of 20 physical ailments.[2]

In regard to predictors of posttreatment distress, a longitudinal, observational study of 151 women with early-stage breast cancer found that physical symptoms and side effects experienced during treatment were predictive of posttreatment cancer-related distress, amounting to 6% of the total 24% of variance accounted for.[9] In addition, demographic variables associated with this posttreatment cancer-related distress included younger age, nonwhite racial status, and less formal education. Clinical variables associated with distress included having a mastectomy rather than lumpectomy, receiving hormonal treatment, and the presence of a diagnosable mental disorder at the time of recruitment into the study.

A comprehensive analysis of prospective studies investigated predictors of longer-term distress (≥ 12 months from the time of diagnosis).[4] This analysis found that a higher level of distress around the time of diagnosis is the most reliable predictor of longer-term heightened distress.

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Screening and Assessment

Screening and assessment have been viewed as two distinct processes.[1,2] Screening is a rapid method of identifying patients with psychosocial distress and is typically conducted by non-mental-health professionals using brief self-report questionnaires to determine whether an individual needs referral for more-extensive assessment.[3] The psychosocial assessment of the cancer patient is a more in-depth clinical interview focused on factors relevant to coping and adaptation. Mental health professionals conduct the assessment interview to determine how well a patient is adjusting.[1]

Self-Report Screening Instruments

Studies have tested the ability of single-item measures to accurately identify patients in distress.[4-8] In general, these ultrashort screening methods, such as the Distress Thermometer (DT), have demonstrated only modest overall accuracy. They are best for ruling out—but performed poorly at confirming—distress, anxiety, and depression.

The Distress Thermometer (DT)

The DT, the National Comprehensive Cancer Network (NCCN) single-item and rapid-screening instrument, asks patients to rate their distress on a scale of 0 to 10, with 10 being extreme distress. On an accompanying problem checklist, patients are asked to indicate what has been a problem for them in the past week.[9] Although many screening instruments have been tested with cancer patients, the DT has been the most widely investigated. The psychometric properties of the DT—a 0-to-10 visual analog scale in the form of a thermometer labeled *No distress* at 0 and *Extreme distress* at 10—have been investigated.[4]

The DT was found to have reasonable convergent and divergent validity when compared with two well-established, multidimensional symptom inventories. This very brief rapid-screening procedure has a moderate ability to accurately detect distress as defined by scores indicative of *caseness* on the two-symptom inventories. When specific cutoff scores were tested to maximize sensitivity and specificity, no single cutoff that maximized the accuracy of classification was discovered. Thus, it was recommended that varying cutoff scores result in different referral recommendations, such that low scores result in no referral, moderate scores result in an optional referral, and high scores result in a strong recommendation for further interventions.[4]

A study of 321 women with newly diagnosed stage I to stage III breast cancer investigated the ability of the single-item DT to specifically predict depression, as measured by a self-report questionnaire of the nine symptoms of major depressive disorder found in the fourth revised edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV-TR). Sensitivity and specificity characteristics were evaluated, and the optimal cutoff score of 7 was identified, resulting in a sensitivity of 0.81 and a specificity of 0.85 for detecting depression. Therefore, individuals scoring 7 or higher should undergo a more-thorough psychosocial evaluation.[10]

Other self-report screening instruments

Many other self-report questionnaires have been used as screening instruments (refer to Table 1); in general, they also are better for ruling out distress and perform poorly at confirming distress. Thus, most screening instruments will yield a high number of false-positive results and need to be followed by a more-extensive psychosocial assessment interview.

Table 1. Examples of Self-Report Screening Instruments Used for Identification of Psychosocial Distress in Cancer Patients

Title	Items (no.)	Time (min)	Constructs Measured
Brief Symptom Inventory (BSI) [11]	53	7–10	Somatization, anxiety, interpersonal sensitivity, depression, hostility, phobic anxiety, paranoid ideation, psychoticism, and obsessive-compulsiveness
Brief Symptom Inventory (BSI-18) [12]	18	3–5	Somatization, depression, anxiety, and general distress
Distress Thermometer (DT) and Problem List [2,10]	Varies	2–3	Distress and problems related to the distress
Functional Assessment of Chronic Illness Therapy (FACIT)	27	5–10	4 domains of quality of life: physical, functional,

formerly the Functional Assessment of Cancer Therapy [FACT]) [13]			social/family, and emotional well-being
Hospital Anxiety and Depression Scale (HADS) [14-16]	14	5-10	Emotional-cognitive symptoms of clinical depression and anxiety without neurovegetative symptoms
Patient-Reported Outcomes Measurement Information System (PROMIS) screeners [17]	Up to 88 (8-15 per domain)	Varies	Clinical norms based on age, cancer stage, and cancer type across 8 domains (anxiety, depression, pain interference, fatigue, sleep disturbance, physical functioning, social functioning, and cognitive functioning); each domain can be given separately
Profile of Mood States (POMS) [18]	65	10-25	6 mood states: anxiety, fatigue, confusion, depression, anger, and vigor
Zung Self-Rating Depression Scale [19]	20	5-10	Symptoms of depression

Self-report screening instruments must be scored, evaluated, and discussed with each patient. Triage—the process of communicating screening results, discussing each patient’s needs, and determining the best course of further action—is key to the successful use of screening. In fact, screening without availability of appropriate treatment resources is considered unethical. The primary oncology team (oncologist, nurse, palliative care specialist, social worker, and counselor) is responsible for successful triage. In some studies, a significant percentage of patients who report moderate to high levels of distress refuse further assessment. [20-23] The primary oncology team should consider how best to introduce the need for further psychosocial

assessment.

The NCCN standards of care [9] suggest that distress rated as mild might result in a referral to a local self-help group or management by the primary oncology team only. Distress rated as moderate to severe warrants referral to other appropriate professionals (psychologists, psychiatrists, social workers, palliative care specialists, or pastoral counselors), depending on the nature of the distress.

Psychosocial Assessment

The assessment of psychosocial adaptation should follow screening when distress is identified. The psychosocial assessment is typically a semistructured interview during which the professional evaluates how well an individual patient, a patient's family, and other significant people in a patient's life are adapting to the current demands of the illness. In general, this assessment process considers a wide variety of factors relevant to overall adaptation.[1] (Refer to the [General Factors Influencing Adjustment](#) section of this summary for more information.)

A successful transition from screening to assessment involves clear communication between the oncology team and the patient. Although there is no single best way to talk to patients about psychosocial needs, clinical experience suggests some important concepts. First, most patients will respond to the recommendations of health care professionals who exhibit trust, expertise, warmth, care, and concern.

Choice of words is important. Words that suggest the stigma of serious mental illness, such as *psychiatric*, *psychological*, *mental disorder*, *maladjustment*, or *mental illness*, should be avoided—in favor of words such as *distress*, *concerns*, *worries*, *uncertainties*, or *stressors* from the illness or its treatment. Suggestions for word choice include the following:

- The questionnaire you filled out helps us to understand you as a whole person, and we want to provide the best care possible for you—physically, emotionally, socially, and spiritually.
- As you may realize, a serious illness can affect the quality of your life in many ways (emotionally, socially, financially, and in regard to work, relationships, and energy). There is much more to this illness than just the physical, and we want to be sure we are addressing these other dimensions of your life.
- Your concerns and worries are very understandable, given your illness and its treatment. We don't want to ignore the (emotional, social, spiritual) aspects of your experience right now.
- We have found that many patients benefit greatly from a chance to talk further about their concerns with a health care professional (e.g., social worker, mental health professional, palliative care specialist, or pastoral counselor), and we would like to schedule that for you.
- For further explanation, we suggest an interview that lasts about 45 minutes with a professional who will:
 - Listen closely to you.
 - Want to know about your experiences with your illness.

- Ask about you, your family and friends, and other support persons.
- Ask about how you have been adjusting to your illness and may encourage you to continue (and give you feedback about) successful coping strategies you are already using.
- Suggest additional ways to address your concerns.

Model Screening Programs

Various comprehensive cancer centers have developed models for screening for psychosocial distress. Although there are notable differences, most models involve the following sequential steps:

- Screening administration.
- Scoring and evaluation.
- Referral.

Most screening for psychosocial distress focuses on the individual patient; however, some family-focused screening procedures are being developed.[\[24\]](#)

Administration of a screening instrument involves a 5- to 10-minute process in which each patient answers a series of simple, straightforward questions about distress, either orally or via a self-report paper-based questionnaire or computer questionnaire. Answers are scored and evaluated on the basis of previously determined criteria. If scores fall above the defined criteria, then a formal referral to the appropriate discipline (social work, psychology, psychiatry, palliative care, or pastoral care) is made. Distress management then begins with a more-comprehensive face-to-face psychosocial assessment interview [\[1\]](#) by a qualified health care professional (e.g., social worker, psychologist, psychiatrist, palliative care specialist, or pastoral counselor) appropriate to the issues identified.

The success of screening programs can be measured in terms of the following outcomes:

- Accurate identification of patients who are experiencing significant psychosocial distress.
- Improved referral of patients to appropriate health care professionals to address clinically relevant distress.
- Acceptance of such referrals by patients who are experiencing high-level distress.
- Improved patient-clinician communication, with frequent discussion of quality-of-life issues during patient visits.
- Decreased level of distress and improved quality of life resulting from the screening program.

Few empirical studies have evaluated the impact of structured screening programs using these outcomes. In most of these studies, intervention included telephone follow-up of screening results with referrals or in-person discussions with clinicians, trained or untrained in screening. Study designs have differed in terms of

screening tools (brief vs. comprehensive screening tools), intervention components (trained vs. untrained screening clinicians), and study outcomes. Study designs have also differed in their controls; for example, control groups in some studies did not undergo screening,[25] while others involved patient screening but with no screening results conveyed to clinicians.[26]

The results of the screening studies have been mixed, depending on the structure of the screening programs and the assessed outcomes. Two studies found no meaningful differences between control and intervention groups in distress, quality of life, or cancer needs.[25,26] Low patient acceptance of psychosocial referral services was one of the limitations identified in these studies.[26]

In one study, a subgroup of moderately to severely depressed patients showed a significant reduction in depression after the intervention,[26] while another study concluded that the best predictor of decreased anxiety/depression was referral to psychosocial services.[27] Another study showed the feasibility of implementing a personalized as well as a computerized screening program in a large patient population (N = 3,133) at a tertiary cancer center.[28]

Given these mixed results, further empirical evaluation of the effectiveness of screening programs is necessary. The following examples will help to illustrate the process.

Memorial Sloan-Kettering Cancer Center has experimented with the DT, which was modeled after tools used to measure pain.[9] The descriptive anchor points on the DT include the following:

- *No distress* at a rating of 0.
- *Extreme distress* at a rating of 10.

Patients are asked to rate the distress they have been experiencing in the past week, including the day of the screening, on a scale of 0 to 10. Accompanying the DT is a problem checklist that helps identify relevant potential sources of stress. The patient is asked to check the problems that are most relevant. Categories of problems include the following:

- Practical (e.g., housing, insurance, or transportation).
- Physical (e.g., pain, nausea, or fatigue).
- Family or support (e.g., partner, children, or friends).
- Emotional (e.g., worry, sadness, depression, or anger).
- Spiritual/religious (e.g., relating to God or loss of faith).

The primary oncology team (oncologist, nurse, palliative care specialist, and social worker) is responsible for administering this brief screening, evaluating a patient's response, and arranging for a referral, when necessary. Preliminary testing of this procedure used a cutoff score of 5 or higher as requiring further evaluation. Initial needs assessments have shown that 20% to 52% of patients report significant levels of

distress.[9]

At Johns Hopkins Cancer Center, all new patients receive an 18-item version of the Brief Symptom Inventory (BSI),[12] which lists 18 problems people sometimes experience (e.g., feeling faint or dizzy, having no interest in things, loneliness, or nausea or upset stomach). Patients are asked how much they were distressed by each of the 18 problems during the past 7 days, including the day of the screening. The procedure is automated and utilizes existing clerical and support staff to distribute and retrieve the inventory during the first or second visit.[2] After computerized scoring is completed, professional staff is involved when offers for services are being provided. Patients screened as having high levels of distress are referred to a social worker for immediate follow-up; those screened as having low levels of distress are referred to the psychosocial orientation program, which is a structured educational program designed to enhance the adaptation of patients by providing information about a range of psychosocial programs (e.g., disease-specific support groups or psychoeducational presentations).

The Oncology Symptom Control Research group at Community Cancer Care typically screens all incoming patients with the Zung Self-Rating Depression Scale (ZSDS).[29,30] The ZSDS is a 20-item self-report depression screen that has been used to detect depression and more-general distress; single items are also used to screen for conditions such as fatigue.[31] Staff typically administer the screen while patients are in the waiting room. Scores are analyzed immediately after completion so that the medical oncologists can be briefed on any pertinent issues. In addition, patients scoring in the moderate range or higher are identified for further follow-up and more-extensive interviews and assessment by the staff psychiatrist or psychologist. Also, patients who trigger single items of interest, such as fatigue, are interviewed and monitored for possible inclusion in a number of symptom-control research trials.

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Normal Adjustment

Adjustment, well-being, or psychosocial adaptation to cancer has been defined [1-3] as an ongoing process in which the individual patient tries to manage emotional distress, solve specific cancer-related problems, and gain mastery of or control over cancer-related life events. Adjustment to cancer is not a unitary, single event but rather a series of ongoing coping responses to the multiple tasks associated with living with cancer. Patients are faced with many challenges that vary with the clinical course of the disease. Common periods of crisis and significant challenge include the following:

- Initial diagnosis.
- Active treatment (surgery, radiation, and chemotherapy).
- Posttreatment and remission.

- Recurrence.
- Terminating curative treatment.
- Long-term survivorship.

Each of these events includes certain coping tasks, particular existential questions, many common emotional responses, and specific problems.

Normal or successful adjustment is indicated in patients who are able to minimize disruptions to life roles, regulate emotional distress, and remain actively involved in aspects of life that continue to hold meaning and importance.

Coping refers to the specific thoughts and behaviors that patients use in their efforts to adjust.[2] One cognitive theory of coping [4] proposes that in response to significant life events, a person asks two important questions:

- Is this event personally significant to me?
- What resources do I have to manage/control this event?

A low level of distress is the result of a perception that either the demands of a situation are very low or the individual's resources are substantial.[5] Therefore, to lower distress levels, either the perceived demands of a situation should be lowered, or the perceived resources should be increased.

Coping strategies refer to specific cognitive and behavioral activities that use situation-specific coping efforts, such as readjusting one's daily routine or work schedule to adjust to the side effects of cancer treatment. Coping strategies comprise efforts to adjust. Among many successful coping strategies, three broad categories have been noted:[2,6,7]

- Problem focused.
- Emotion focused.
- Meaning focused.

Patients may switch between these strategies, even from adaptive to maladaptive, depending on their current functioning levels.

Problem-focused strategies help patients manage specific problems by directly trying to alter problematic situations. Some of these approaches may be adaptive (e.g., seeking information about treatment option survival rates), but some problem-focused strategies may not be adaptive (e.g., paying large amounts of money for unempirical treatment options).[8] *Emotion-focused strategies* help patients regulate their degree of emotional distress with either emotion-engaging behaviors (e.g., seeking social support); or emotion-avoidant behaviors, as the person attempts to escape reminders of the cause of the distress (e.g., not seeking

treatment after a diagnosis, use of alcohol or other drugs). *Meaning-focused strategies* help patients understand why this has happened and what impact cancer will have on their lives. In general, people who adjust well typically remain committed to and actively engaged in the process of coping with cancer and continue to find meaning and importance in their lives. Conversely, people who do not adjust well often become disengaged, withdraw, and feel hopeless. Thus, assessing the degree of engagement versus giving up may be a way to distinguish between successful and unsuccessful adjustment.

Coping style refers to the most-common, more-frequent, and longer-term use of a set of coping strategies (e.g., use of alcohol, seeking social support, use of religious/spirituality resources) that an individual tends to use across a variety of life situations. Coping style is often closely related to overall disposition and personality (e.g., optimism, pessimism, introversion, extroversion).[9]

One criticism of the literature on coping with cancer focuses on the assumption that *coping with cancer* is a unitary, single event. In reality, coping with cancer involves coping styles and strategies that may differ and vary according to the nature of the stressors being encountered. For example, in a study of 52 adults receiving palliative care for cancer,[10] patients participated in a semistructured interview during which they were asked how they coped with their most significant stressors. Results showed that most participants used a range of coping strategies; however, there were interactions between stressor domains (existential, psychosocial, physical) and coping categories (problem focused, emotion focused, emotion avoidant). Problem-focused strategies were used less frequently for the existential stressors, while emotion-focused strategies were used less frequently for the physical stressors.[10]

General Factors Influencing Adjustment

Although there are some commonalities in normal adjustment to the varying stressors of cancer, there are also many individual differences. It is difficult to predict how individuals will cope with cancer, so it is important to recognize factors that influence adjustment to cancer. One study of women with stage II or stage III breast cancer [11] reported that higher levels of stress (including both cancer and noncancer stressors) measured postsurgically at the time of diagnosis predicted lower physical and psychological quality of life.

Another study evaluated women with stage 0 to stage III breast cancer (N = 89) at three time points: during treatment, 3 weeks following the end of treatment, and 3 months posttreatment. Most survivors showed good adjustment on general distress indices. The factors predicting sustained distress included younger age, history of depression or anxiety, and more-extensive treatment.[12]

Psychosocial adjustment/adaptation is influenced by three broad categories of factors: cancer derived, patient derived, and society derived.[3]

The personality traits of optimism and pessimism might play a critical role in the psychological well-being of cancer patients. A German study investigated the impact of optimism and pessimism on psychological well-being in 161 newly diagnosed cancer patients with heterogeneous cancers.[13] Patients were assessed for

optimism/pessimism and positive/negative emotions before the start of their first chemotherapy session and at 9 months' follow-up. Before the start of chemotherapy, psychological well-being was associated with higher levels of optimism and lower levels of pessimism. At the 9-month follow-up, pessimism predicted negative changes in psychological well-being as well as heightened experiences of chemotherapy-related side effects.

The availability of social support has been found to be related to mortality from breast cancer. In a longitudinal study of 2,835 female nurses with breast cancer, those who reported no close contacts (e.g., relatives, friends, or living children) before their diagnosis had a twofold increased risk of mortality from breast cancer, compared with those who had more social contacts (e.g., ten or more close relatives).[14]

Situation-Specific Influences on Adjustment

Hearing the diagnosis

The process of adjusting to cancer can begin even before a diagnosis. Patients may respond with normal levels of fear, worry, and concern when they have unexplained symptoms or when they realize that they are undergoing testing to determine the presence of cancer. When they hear the diagnosis, their fears become realized, generating a psychological and existential plight (crisis).[15] Because of the effect that heightened distress secondary to adjustment to cancer can have on attention and cognitive processing, communication with patients about their cancer diagnosis may be impaired (refer to the PDQ summary on [Communication in Cancer Care](#) for more information).[16] Additional professional support to address problems such as fatigue, insomnia, and depressed mood that are associated with adjustment to cancer and may also affect patient-provider interactions and quality of life can be helpful during this time.[17]

Active treatment

Longer-term adaptation consists of the extended time during which more long-lasting and permanent adjustment occurs. This period consists of weeks and months during which patients utilize a variety of coping strategies and styles. This combination of longer-term coping styles and short-term coping strategies usually serves patients well in their efforts at adaptation.[18] The individual differences that patients bring to their encounters with cancer will result in varied coping styles and strategies, both adaptive and maladaptive.[19]

Posttreatment remission

The completion of active treatment can cause ambivalence for cancer patients and their families. The completion of active treatment can be a time of heightened distress,[20] with a renewed sense of vulnerability that comes with the cessation of active medical efforts to fight the disease, decreased monitoring, and loss of frequent contact/support from the medical team.[21]

Other adjustment issues include living with uncertainty, returning to previous life roles, and hypervigilance to health concerns, especially if the cognitive or physical effects of cancer or treatment linger.[22]

Normal anxiety and worry often intensify as the dates of follow-up appointments approach. Normal anxiety

comes from concerns about recurrence and the related emotional consequences (e.g., re-entry into the patient role and renewed feelings of loss of control). Many patients find waiting for test results to be a particularly distressing experience.

For most individuals, adjustment to completing treatment causes a normal escalation of distress, but this appears to be temporary and resolves within a few weeks for many patients. In an empirical study of posttreatment adjustment, 94 women with stage 0, I, II, or III breast cancer who were completing radiation therapy were assessed on measures of depression, anxiety, and quality of life on the last day of treatment and at 2 weeks, 4 to 6 weeks, 3 months, and 6 months posttreatment. Results found elevated symptoms of depression, low-level anxiety, and diminished quality of life on the last day of treatment; however, by 2 weeks later, symptoms of depression decreased significantly, and quality of life improved significantly.[23]

Recurrence

Recurrence of cancer after treatment can escalate stress for patients and may prompt providers to screen for psychosocial-spiritual distress. In a study of women with recurrent breast cancer, significant impairments in physical, functional, and emotional well-being were found within 1 month after recurrence; however, a patient's self-efficacy (confidence in an ability to manage the demands of illness), social support, and family hardiness (family's internal strength and ability to manage hardship and change) had positive effects on quality of life. Conversely, more distress about physical symptoms, additional life concerns, a sense of hopelessness, and a negative perception of illness or caregiving were associated with a lower quality of life. [24]

Terminating curative treatment

The transition from a curative treatment plan to one more focused on palliative care can be extremely difficult for cancer patients. Extreme anguish can accompany this transition, as the patient faces renewed psychological distress, physical symptoms, and the existential crisis of death, all of which combine to result in the suffering often associated with advanced cancer.[25] A meta-analysis examined mental health variables in 24 studies of mood disorders in palliative care settings that were done in seven countries with more than 4,000 patients.[26] Diagnoses in all of the studies were made via criteria of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) or the *International Statistical Classification of Diseases and Related Health Problems* (ICD). This meta-analysis found that while mood disorders and anxiety were prevalent in palliative care patients—and should certainly be screened for and treated in any palliative care setting—it is not abnormal for patients to have no mental health concerns during palliative care treatment. Major mood disorder or depression was found in 24.6% of the palliative care population, while some form of anxiety disorder was identified in almost 10% (9.8%) of patients. Milder forms of mental health concerns, such as adjustment disorder (with anxiety and/or depressive features), were found in 24.7% of patients.[26] (Refer to the PDQ summaries on [Depression](#) and [Cancer-Related Post-traumatic Stress](#) for more information.)

The patient who successfully adjusts to the crisis of recurrence often shifts expectations and maintains hope in a variety of meaningful life activities. For example, a patient who has confidence that pain and suffering

can be controlled will have hope for future quality of life. Religion and spirituality play a very important role in helping many patients maintain mental and physical quality of life. As with screening for physical and mental health conditions that may interfere with quality of life, providers may wish to screen for spiritual health as part of the adjustment to this stage of cancer in order to make appropriate referrals.[27,28] (Refer to the PDQ summary on [Spirituality in Cancer Care](#) for more information.)

Long-term survivorship

The adjustment from posttreatment to long-term survivorship is gradual and extends over many years. However, most patients, despite various cancer diagnoses and treatments, adjust well, with some even reporting benefits to a cancer diagnosis (e.g., greater appreciation of life, reprioritizing of life values, strengthening of spiritual or religious beliefs).[29-32] Patients who have poorer adjustment tend to have greater medical problems, fewer social supports, poorer premorbid psychological adjustment, and fewer economic resources.

In general, studies of cancer survivors and healthy comparison groups have found no significant differences in measures of psychological distress, marital and sexual adjustment, social functioning, and overall psychosocial functioning.

However, many cancer patients experience some common areas of distress that are subthreshold or not severe enough to meet diagnostic criteria, including anxiety about recurrence, an increased sense of vulnerability, lowered sense of control, conditioned reminders of chemotherapy (smells, sights) that produce anxiety and nausea, post-traumatic stress-like symptoms (such as persistent, intrusive thoughts or recurrent imagery associated with cancer), fatigue, and concerns about body image and sexuality.[33] An assessment of more than 6,000 cancer survivors found that more than 50% reported fear of recurrence, mostly with low intensity. Survivors at risk of experiencing high levels of fear of recurrence included women survivors, individuals younger than 59 years, those at 5 to 7 years postdiagnosis, the socially isolated, those with lower education levels, and individuals with a history of metastases or recurrence.[34]

In one of the few prospective longitudinal studies of cancer survivors, 752 patients from three U.S. states were asked about a variety of psychosocial problems. About 1 year after diagnosis, 68% felt fearful that their illness would return, approximately 60% were concerned about relapsing, and 58% had fears about the future. In addition, approximately two out of three survivors were concerned about a physical health problem, such as fatigue and loss of strength. Approximately 48% reported sleep difficulties, and 41% reported concerns with sexual dysfunction. Younger survivors (aged 18–54 years), women, nonwhites, unmarried survivors, and those with lower incomes reported more problems. In comparisons of four common cancers, the most concerns regarding problems in living were reported by those with lung cancer, followed by survivors of breast, colorectal, and prostate cancers.[35]

Multifocal interventions may help cancer survivors address multiple mental and physical health issues simultaneously. In a multicenter trial of 222 posttreatment breast cancer survivors, researchers implemented the Better Exercise Adherence after Treatment for Cancer (BEAT Cancer) intervention. In this study, over 3

months, patients engaged in 12 supervised exercise sessions that were tapered to an unsupervised at-home exercise program (though logged with a heart rate monitor), individual counseling sessions, and group counseling. These sessions encouraged regular exercise, promoted self-monitoring, and engaged patients in cognitive reframing of current physical limitations, which had a significant positive impact on body image, mood, cardiovascular fitness, and general quality of life.[36]

A large (N = 660) longitudinal study of women breast cancer survivors older than 65 years investigated factors associated with changes in emotional well-being. Overall findings suggested that the 5-year survivorship experience for most women is relatively stable, with few changes in emotional well-being. However, it was noted that women who had fewer than 12 years of formal education and women who perceived themselves as never being cured were more likely to experience declines in emotional well-being, while those who had better physical functioning, good emotional support, and the perception of positive physician-patient communication were less likely to have poor emotional health.[37]

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Psychosocial Distress

Distress has been defined as “a multifactorial unpleasant experience of a psychological (i.e., cognitive, behavioral, emotional), social, spiritual, and/or physical nature that may interfere with the ability to cope effectively with cancer, its physical symptoms, and its treatment. Distress extends along a continuum, ranging from common normal feelings of vulnerability, sadness, and fears to problems that can become disabling, such as depression, anxiety, panic, social isolation, and existential and spiritual crisis.”^[1] Standards of care have been developed for the management of psychosocial distress.^[2]

The broad goal of the National Comprehensive Cancer Network (NCCN) is to establish standards of care so that all patients experiencing psychosocial distress will be accurately and routinely identified, recognized, and

treated.[1] NCCN guidelines include recommendations for the following:

- Screening.
- Triage.
- Initial evaluation.

Also included are referral and treatment guidelines for each participating profession:

- Mental health (psychology and psychiatry).
- Social work.
- Palliative care.
- Pastoral care.

The times most likely to require screening include the following periods during the illness when distress is most likely to occur:

- Shortly after diagnosis.
- At the start of treatment (surgery, radiation, and chemotherapy).
- At the conclusion of a long course of treatment.
- Periodically during posttreatment and remission.
- At the time of recurrence.
- With transition to palliative care.

(Refer to the [Overview](#) section of this summary for more information.)

Psychosocial Interventions for Distress

The efficacy of psychosocial interventions for adult cancer patients is supported by an extensive body of literature.[3][[Level of evidence: IV](#)];[4-6][[Level of evidence: I](#)] Reviews have concluded that, in general, psychosocial interventions for cancer patients have shown positive benefits.

Psychosocial interventions have generally been defined as nonpharmacologic interventions that include a variety of psychological and educational components. Typical components include the following:

- Relaxation training.
- Cognitive and behavioral coping strategies.
- Cancer education/information sessions.
- Existential therapy.

- Group social support.

Interventions have included various combinations of these components, have varied in length (single session to multiple weekly sessions), and have been administered in both individual and group formats. The most common patient population has been U.S. white women of middle to higher socioeconomic status who have breast cancer; however, some studies include mixed cancer diagnoses, and studies from European countries have appeared.[3] Outcome measures have varied and have included the following:[3,4]

- Emotional adjustment (e.g., depression, anxiety).
- Functional impairment (e.g., return to work, social roles).
- Disease-related symptoms (e.g., nausea/vomiting, fatigue, pain).
- Health behaviors (e.g., diet, smoking, exercise).
- Immune system functioning.

A biobehavioral model [3] hypothesizing psychological, behavioral, and biologic pathways from cancer stressors to disease outcome has guided much of this research; however, the most common outcome measured has been emotional adjustment.

Although positive benefits have been found, their clinical significance has been questioned. Reviewers have offered varying conclusions regarding the size of these positive effects,[4][[Level of evidence: I](#)] ranging from negligible for depression, to small for overall emotional outcomes, to moderate for anxiety.[5][[Level of evidence: I](#)]

Effect sizes may be related to the timing of the intervention and patient selection procedures. For most patients, levels of psychosocial distress are highest during the earliest days of their cancer experience and, for many, dissipate quickly. Thus, if interventions are offered later in the cancer experience (weeks or months after diagnosis and treatment), patients may be experiencing less distress than they would have experienced if interventions had been offered earlier, making large effects more difficult to detect.[7][[Level of evidence: II](#)]

In one study,[8] 249 breast cancer patient-partner dyads were randomly assigned to one of four groups:

- A control group that received standard disease management.
- A standardized psychoeducation group.
- A group that received telephone counseling.
- A group that received psychoeducation plus telephone counseling.

Patients and partners who received the study interventions had less side-effect distress and severity as well as higher levels of psychological well-being than did those who received standard care. In addition, the study results support the efficacy of low-cost, replicable interventions by video and telephone to achieve these

physical and psychological benefits.[8]

Two meta-analyses [4,5][[Level of evidence: I](#)] report the following effect sizes:

- 0.19 for depression [5] and functional adjustment.[4]
- 0.24 for emotional adjustment.[4]
- 0.26 for treatment- or disease-related symptoms.[4]
- 0.28 for global measures of outcome.[4]
- 0.36 for anxiety.[5]

These positive effect sizes indicate that the average patient receiving the intervention is better off than between 57% and 65% of those not receiving the intervention.

In summary, it appears that when psychosocial interventions are offered to patients who are found to be experiencing distress (e.g., anxiety, depression), the efficacy of the intervention is very strong. Thus, the overall positive benefit for psychosocial interventions seems to be greater with those who seem to need it most.[4,5]

Randomized trial of group interventions for breast cancer

The study described below is representative of randomized clinical trials testing the efficacy of small-group psychosocial interventions for U.S. women with early-stage breast cancer. Studies vary in total treatment time, from 8 hours [9][[Level of evidence: I](#)] to 20 hours [7,10][[Level of evidence: II](#)] to 27 hours,[11][[Level of evidence: I](#)] and have a variety of intervention components. (Refer to the [Group counseling](#) section in [The Adjustment Disorders](#) section of this summary for more information.)

Investigators evaluated an educational intervention consisting of 2-hour once-per-month group sessions for 4 consecutive months.[9][[Level of evidence: I](#)] Participants were 252 women younger than 50 years with early-stage breast cancer, who had recently completed nonhormonal adjuvant treatment, and who were facing the transition from active treatment to posttreatment survivorship. They were randomly assigned to one of three groups:

- A standard medical care group.
- A nutrition education group.
- A psychosocial education group.

The psychosocial and nutrition education groups included information dissemination, discussion, and some activities/exercises. Topics rotated monthly, and participants could join a group at any time (i.e., they were open groups). In general, patient-to-patient interaction was minimal because sessions were more didactic presentations. The psychosocial education group presented topics relevant to younger women with breast

cancer, such as the following:

- Talking with children about cancer.
- How to carry on with life after a diagnosis.
- Relationships/intimacy with partners.
- Hormones and cancer.
- Genetic bases of breast cancer.

The nutrition education group included information about choosing fruits, vegetables, and low-fat foods and how to consistently incorporate these foods into daily life. Shopping, low-fat cooking, eating out, and other related topics were presented. Results showed that patients in both of the intervention groups reported fewer depressive symptoms and better physical functioning at a 13-month follow-up. This study is an example of a more-targeted intervention designed for a specific patient population (younger women with breast cancer) at a specific time in their treatment course (soon after completion of active treatment).

Self-administered stress management training for chemotherapy

In a randomized trial of 411 mixed-diagnosis cancer patients,[12][Level of evidence: I] traditional psychosocial care was compared with professionally administered and self-administered stress management for chemotherapy. The professional stress management consisted of a 60-minute individual educational session that included a review of common sources of chemotherapy-related stress and three specific stress-management techniques:

- Paced abdominal breathing.
- Progressive muscle relaxation with imagery.
- The use of coping self-statements.

The professional provided the patient with an audiotape of the individual session, prescribed daily practice of the three techniques, and met briefly with the patient before his or her first chemotherapy session.

In the self-administered group, a professional met with each patient for approximately 10 minutes, provided him or her with a packet of instructional materials about coping with chemotherapy, and briefly instructed the patient on their use. These materials included all of the same information provided in the professionally administered group plus the following:

- A 15-minute videotape.
- A 12-page booklet.
- A 35-minute relaxation audiotape.

Patients in this group were instructed to first view the videotape and then review the booklet, following its

instructions for further training, practice, and use of the various techniques.

Results of this novel approach found that patients in the self-administered intervention reported significantly better physical functioning, vitality, and mental health and fewer role limitations than those reported by either of the other two groups. Patients in the professionally administered group reported no better outcomes than did patients in the traditional-care group. Costs of the self-administered group were found to be significantly lower than those of the other two groups.

Brief orientation and tour of a medical oncology clinic

A novel intervention tested the effects of a brief (15- to 20-minute) clinic tour for new patients in a medical oncology clinic.^[13][\[Level of evidence: I\]](#) The tour included the following:

- An opportunity to see the phlebotomy, nursing, and chemotherapy areas.
- The distribution of written materials about clinic hours and procedures.
- A time to ask questions.

One hundred and fifty consecutively referred patients who had a variety of cancers were randomly assigned to either the clinic orientation intervention or standard care. Intervention patients showed less anxiety, less mood disturbance, and fewer depressive symptoms at a 1-week follow-up. In addition, these patients reported more knowledge of clinic procedures, more confidence in their physicians, and higher levels of satisfaction and hope. This is an example of how even a simple, minimal intervention can have positive benefits.

Use of online information

The Comprehensive Health Enhancement Support System (CHESS) ^[14] is an online resource for cancer patients. It has two components:

1. Didactic material.
2. Narrative information about medical, practical, and psychosocial issues.

This study addressed the relative appeal and value of these two components separately for white and African American women who had been diagnosed with breast cancer (three-fourths of participants had early-stage disease). The average time spent online with either type of resource was slightly longer for African American women (didactic: 19.7 minutes, standard deviation [SD] = 31.10; narrative: 17.16 minutes, SD = 38.19) than for white women (didactic: 18.30 minutes, SD = 28.62; narrative: 15.78 minutes, SD = 36.60) but had substantially more effect.

Before using the resource, African American women were markedly lower in health care participation; after use, African American women increased health care participation markedly, regardless of the type of resource, and surpassed the level of health care participation by white women, particularly in regard to the

effect of the didactic services. This result suggests that while the use of both the didactic and narrative CHES resources is valuable for both groups, it is particularly useful for African American women; the narrative resource version appears to differentially have more impact for white women.

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The Adjustment Disorders

The adjustment disorders are a diagnostic category of the fifth edition of the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5),^[1] defined as reactions to an identifiable psychosocial stressor (e.g., cancer diagnosis or transition in care). The reactions occur within 3 months of the onset of the stressor with a degree of psychopathology that is less severe than diagnosable mental disorders, such as major depressive disorder or generalized anxiety disorder, and yet are "in excess of what would be expected" or result "in significant impairment in social or occupational functioning." Four of the most common subtypes are (1) with depressed mood, (2) with anxiety, (3) with anxiety and depressed mood, and (4) with mixed disturbance of emotions and conduct (for patients who may be showing behavioral signs of an adjustment disorder, such as missing appointments or new substance abuse).

Prevalence

Nearly every cancer patient experiences what could be considered an identifiable stressor, whether that is diagnosis, treatment, recurrence, or side effects. The presence of an adjustment disorder is determined by the patient's response to the identifiable stressor.

Adjustment disorders are the most commonly diagnosed mental health issue in the oncology setting. A meta-analysis examining 70 studies across 14 countries with more than 10,000 participants in active treatment oncology or hematological oncology settings found a prevalence rate of approximately 20% among ambulatory cancer patients in active treatment.^[2]

Additional reviews more focused on North American populations ^[3] have found adjustment disorders to be the most common mental health issue among cancer patients. In patients with advanced cancer, prevalence ranges from 14% to 34.7%; in terminally ill patients, rates range from 10.6% to 16.3%. These variable prevalence rates are influenced by stage of disease, type of cancer, diagnostic procedures used, and other patient variables. In a study of women with breast cancer undergoing adjuvant chemotherapy, a 36.1% prevalence rate was found.^[4]

Treatment

Although few studies are targeted specifically at a population of cancer patients diagnosed exclusively with adjustment disorder, a number of studies have shown the benefits of psychosocial interventions with adult cancer patients (e.g., meta-analysis).^[5][\[Level of evidence: I\]](#) These interventions have included both individual counseling ^[6][\[Level of evidence: I\]](#) and group counseling,^[7][\[Level of evidence: IV\]](#);^[8,9][\[Level of](#)

evidence: I] and have utilized a variety of theoretical approaches.

Group counseling

Investigators tested the efficacy of a 10-week, 2-hours-per-week group cognitive-behavioral stress management intervention.[10] One hundred newly treated women with breast cancer were randomly assigned to either the intervention or a control condition. The psychosocial intervention consisted of ten 2-hour group sessions during which didactic material was presented, intermixed with a variety of experiential exercises and homework assignments. The overall intervention focused on learning to cope better with daily cancer-related stressors. Topics included progressive muscle relaxation, cognitive restructuring, interpersonal stressor conflict resolution, and social support. The control condition consisted of a day-long seminar in which participants received a condensed psychoeducational version of the intervention, with significantly less interaction among group members. Among intervention participants, results showed a decrease in depression and an increase in benefit-finding (i.e., reporting that having breast cancer had made positive contributions to their lives) and optimism.

In a larger randomized study (N = 199) conducted by the same research group [11] on women with stage 0 to stage III nonmetastatic breast cancer, an intervention similar to that in the first study produced somewhat greater sustained decreases in cancer-related intrusive thoughts and sustained improvements in anxiety.

Another study examined an 18-week, 1.5-hours-per-week group intervention consisting of psychological strategies designed to reduce stress, enhance mood, alter health behaviors (diet, exercise, smoking), and enhance adherence to cancer treatments.[12] Outcome measures included emotional distress, health behaviors, and immune responses. Two hundred twenty-seven women, all of whom had undergone surgery for regional breast cancer, were randomly assigned to either the intervention group or an assessment-only control group. Compared with the control group, the intervention group showed significantly less anxiety, improved ability to access social support, more healthy-lifestyle behaviors (with specific improvements noted in dietary and smoking behaviors), and an improvement in symptom levels and functional status.[12] Furthermore, biobehavioral improvements were identified in immune responses among the intervention group. Improved responses were consistent with the psychological and behavioral changes. This study is a strong example of how psychosocial interventions can create improvements in a variety of biobehavioral (psychological, behavioral, immune) variables.

Mindfulness-based therapy

A randomized controlled trial of a 6-week mindfulness-based stress reduction intervention, compared with usual care, was conducted with 84 female survivors of breast cancer.[13] All participants were within 18 months of completion of surgery, chemotherapy, and/or radiation therapy and were thus in the transitional period from completion of active treatment to posttreatment survivorship. The intervention consisted of weekly 2-hour group sessions conducted by a psychologist who followed a standardized protocol to teach participants sitting meditation, body scan, walking meditation, and gentle yoga. All participants received a training manual and four audiotapes to support home practice and were encouraged to practice daily.

Participants who practiced more frequently showed greater improvements, but all participants in the intervention group showed improvements in psychological measures (fear of recurrence, recurrence concerns, state-trait anxiety, and depression) and quality of life (physical functioning, role limitations, and energy).

In a study examining the efficacy of mindfulness-based stress reduction in breast cancer survivors,[14] 322 subjects were randomly assigned to a 6-week program or usual care. The intervention group received weekly 2-hour sessions consisting of meditative techniques and group processes, and the participating survivors were taught to integrate mindfulness into daily activities. Those who practiced mindfulness-based stress reduction showed improvement in psychological symptoms (anxiety, fear of recurrence overall, and fear of recurrence symptoms) and physical symptoms (fatigue severity and fatigue interference). The survivors with the highest baseline stress experienced the greatest benefit.

In an 8-week study of mindfulness-based cognitive therapy for men with advanced prostate cancer,[15] 94 patients were randomly assigned to a weekly group intervention by telephone and 95 to usual care with minimally enhanced patient education. The 1.25-hour telephone sessions were manualized and included short meditations. Daily home mindfulness meditation was encouraged. There was no difference between groups in psychological or quality-of-life outcomes, and no influence on the use of mindfulness skills apart from observing. The authors suggested that older male populations may be less receptive and responsive to mindfulness.

Hypnosis and relaxation

In one study, a group of women scheduled for excisional breast biopsy (N = 90) were randomly assigned either to a brief session (15 minutes) of hypnosis and guided relaxation delivered by trained clinical psychologists on the day of surgery, or to an attention-control empathic listening session of equal length. Presurgery distress was measured using visual analog scales and the short version of the Profile of Mood States. The hypnosis session markedly decreased anticipatory anxiety and increased relaxation that was measured just before the biopsy was performed, suggesting that hypnosis- and relaxation-naïve patients can receive benefit from brief treatment before stressful situations.[16][Level of evidence: II]

Cognitive-behavioral therapy

Cognitive-behavioral therapy (CBT) has been widely studied. A CBT approach is based on the idea that mental, emotional, and even physical symptoms partly stem from thoughts, feelings, and behaviors, resulting in poor adaptation.[17] Interventions focus directly on a patient's thoughts, feelings, and behaviors with the goal of altering specific coping strategies and alleviating emotional distress. CBT includes a variety of techniques, such as relaxation training, problem solving,[18][Level of evidence: I] cognitive restructuring, and coping self-statements.

Most studies have combined a variety of these approaches into a multicomponent treatment strategy designed to alleviate specific symptoms. CBT approaches tend to be relatively short-term, brief interventions,

well-suited to the oncology setting.[17,18] One study [19][Level of evidence: I] randomly assigned 382 patients with different types of cancer to one of three groups: usual care, professionally led stress management, or self-administered stress management. The two intervention groups received stress management training that included abdominal breathing, progressive muscle relaxation training with guided imagery, and coping self-statements before the start of chemotherapy. The professionally led intervention group met with a mental health professional who taught them the stress management skills in one 60-minute session. The self-administered group received a packet of training materials that included a 15-minute videotape of instructions, a 12-page booklet on coping with chemotherapy, and a 35-minute audiotape of relaxation training instructions. Results showed enhanced quality of life over usual care in the self-administered group only. The professionally led group did not show any improvement in quality of life when compared with usual care.

In a randomized clinical trial for the treatment of adjustment disorders, 57 patients with mixed cancer types were randomly assigned to receive either an 8-week, individual, problem-focused CBT intervention or an 8-week, individual, supportive counseling intervention.[20][Level of evidence: I] Results showed that those receiving the problem-focused CBT exhibited a significant change in fighting spirit, coping with cancer, anxiety, and self-defined problems, both at the conclusion of the intervention and at the 4-month follow-up.

Individual therapy that uses CBT techniques to focus on developing problem-solving skills for use across multiple life stressors has been shown to be useful for cancer patients.[21][Level of evidence: II] In this study, the psychosocial intervention consisted of ten 1.5-hour weekly individual psychotherapy sessions (with or without a significant other present) that focused on training to become an effective problem solver. Four rational problem-solving tasks were emphasized, including formulating the nature of problems, brainstorming alternative solutions, systematically evaluating potential consequences of a solution while deciding on the optimal ones, and evaluating the eventual outcome after solution implementation. Participants in the intervention showed greater problem solving skills, less multidimensional distress, and greater quality of life compared with their control-group counterparts.

A meta-analysis of 45 studies investigating 62 treatment-control comparisons found significant beneficial effects in emotional adjustment for adult cancer patients who participated in psychosocial interventions.[5][Level of evidence: I] Beneficial effect sizes for emotional adjustment ranged from .19 to .28, indicating that the average cancer patient receiving treatment was better off than 56.5% to 59.5% of the patients not receiving treatment. These interventions have been administered in both individual formats [6][Level of evidence: I] and group formats,[22][Level of evidence: II] indicating benefits in emotional adjustment from both formats at the conclusion of the intervention and at 6-month and 12-month follow-up assessments. One novel approach adapted a 6-week group format to a telephone conference-call structure for breast cancer survivors; there were high acceptability and modest treatment effects immediately after the intervention, but not at the 3-month follow-up.[23][Level of evidence: I]

Another study found that a cognitive behavioral intervention to teach problem-solving was effective in promoting better self-management of cancer-related symptoms, especially for patients aged 60 years or

younger.[24][Level of evidence: I]

Increasingly, CBT studies for cancer include biobehavioral outcomes. A three-arm, randomized, controlled trial (N = 159) of a two-session (60–90 minutes) individual CBT-based stress management intervention administered 1 to 2 weeks before radical prostatectomy for men with prostate cancer was found to have a positive impact on a number of immune system parameters (higher natural killer cell cytotoxicity and circulating proinflammatory cytokines).[25][Level of evidence: I] Statistically significant differences in immune outcomes were found only in the intervention group but not in a supportive-attention group or a standard-care group.

Can psychosocial interventions increase survival?

The intriguing question of whether participation in a psychosocial group intervention can result in increased survival has been investigated since 1989. The original study [26] tested a supportive-expressive group therapy format for women with metastatic breast cancer, while another study [27] tested a psychoeducational group intervention for patients with malignant melanoma. In both of these studies, a survival advantage was found in the intervention group. However, a critique of the first study [28] found that members of the control group had significantly shorter survival times than would have been expected, when compared with data from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program, suggesting that the survival advantages may have resulted from inadvertent sampling errors.

Attempts to replicate the supportive-expressive group therapy findings were made in Canada,[29] the United States,[30] and Australia.[31] Although all three studies found significant psychological benefits, no study could replicate the survival benefit.

Literature reviews, including three meta-analyses [32–34] and one systematic review,[35] have concluded that previous research has failed to find an effect of psychotherapy on survival. One summary [36] reported on ten additional randomized controlled trials of various psychosocial interventions for patients with various types of cancers (although most were women with breast cancer). All ten studies noted improved psychosocial benefits. However, nine of the ten showed no significant differences in survival, while one [37] found a survival advantage of about 1 year. This one positive trial was able to stratify groups on a number of important variables (e.g., nodal status, estrogen receptor and progesterone receptor status, and menopausal status) and provided data in support of possible mechanisms, such as enhanced immune functioning and patient compliance with stress reduction procedures. In an analysis of results, this study identified the complexity of factors involved in any survival benefit and the possibility that immune system-mediated benefits may contribute to increased survival when other factors are carefully taken into account.

In summary, the preponderance of evidence indicates that despite evidence of improved quality of life, it seems unlikely that a psychosocial intervention has much chance of showing an independent contribution to survival time. This evidence has led some to suggest that continued research into this question is no longer warranted.[38]

Pharmacotherapy

No studies have specifically targeted a population of cancer patients diagnosed exclusively with adjustment disorder, in which the primary intervention was some form of pharmacotherapy. Given the nature of the adjustment disorders, clinical experience suggests that, if available, an initial trial of short-term counseling or psychotherapy designed to alter or eliminate the identified stressor (and thus alleviate symptoms) should be tried before pharmacotherapy.[39]

As mentioned [previously](#), sometimes the adjustment disorder may progress to a more-severe mental disorder (e.g., major depressive disorder) and thus warrant consideration of pharmacotherapy. In addition, when the patient does not benefit from short-term psychotherapy, adding an appropriate psychotropic medication for a brief period of time (e.g., 2–3 weeks for antianxiety medications, 12 months for antidepressants) may facilitate the psychotherapy, allowing the patient to better employ available coping strategies. The specific pattern of emotional or behavioral symptoms will determine which type of psychotropic medication to consider. (Refer to the PDQ summary on [Depression](#) for more information.)

Current Clinical Trials

Use our [advanced clinical trial search](#) to find NCI-supported cancer clinical trials that are now enrolling patients. The search can be narrowed by location of the trial, type of treatment, name of the drug, and other criteria. [General information](#) about clinical trials is also available.

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Anxiety Disorders: Description and Etiology

Anxiety occurs to varying degrees in patients with cancer and may increase as the disease progresses or as treatment becomes more aggressive.[1] Investigators have found that 44% of patients with cancer reported some anxiety, and 23% reported significant anxiety.[2,3] A meta-analysis examining 70 studies across 14 countries with more than 10,000 participants in active treatment oncology or hematological oncology settings found that, cross-culturally, there appears to be an anxiety disorder prevalence rate of approximately 10% among ambulatory cancer patients in active treatment.[4]

Anxiety reactions that are more prolonged or intense can no longer be classified as adjustment disorders. These disorders can negatively affect quality of life, can interfere with a cancer patient's ability to function socially and emotionally, and require intervention.[5] Anxiety disorders may also be secondary to other aspects of the medical condition, such as uncontrolled pain, certain metabolic states, or medication side effects.

Other specific anxiety disorders—such as generalized anxiety, phobia, or panic disorder—are not as common among cancer patients and usually predate the cancer diagnosis, but these disorders deserve further attention to facilitate cancer care. The stress caused by a diagnosis of cancer and its treatment may precipitate a relapse of preexisting anxiety disorders. These disorders can be disabling and can interfere with treatment. They require prompt diagnosis and effective management.[6]

Factors that can increase the likelihood of developing anxiety disorders during cancer treatment include the following:

- History of anxiety disorders.
- Severe pain (untreated anxiety disorders can also escalate the pain experience).[7]
- Anxiety at time of diagnosis.[8]
- Functional limitations.
- Lack of social support.[2]
- Advancing disease.
- History of trauma.[1,9]

Some medical conditions and interventions are associated with symptoms that present as anxiety disorders, including central nervous system metastases, dyspnea associated with lung cancer, and treatment with corticosteroids and other medications. A patient's experience with cancer or other illnesses may reactivate associations and memories of previous illness and contribute to acute anxiety. Certain demographic factors, such as being female and developing cancer at a young age, are associated with increased anxiety in medical situations.[2,10] Patients who have problems communicating with their families, friends, and physicians are also more at risk of developing anxiety.[10]

Anxiety, on the other hand, can lead to overestimation of negative prognosis. A longitudinal study of women with ductal carcinoma *in situ* (N = 487) found that anxiety as measured by the Hospital Anxiety and Depression Scale was the factor that was most consistently and strongly associated with inaccurate perception of and overestimation of future breast cancer-related risks.[11]

In the patient with advanced disease, anxiety is often caused not by the fear of death but by the issues of uncontrolled pain, isolation, abandonment, and dependency.[12] Many of these factors can be managed when adequately assessed and properly treated.

Anxiety Disorder Caused by Other General Medical Conditions

The following table highlights possible causes of anxiety in cancer patients.

Table 2. Possible Causes of Anxiety^a

Medical Problem	Examples
Poorly controlled pain	Insufficient or as-needed pain medications.
Abnormal metabolic states	Hypoxia, pulmonary embolus, sepsis, delirium, hypoglycemia, bleeding, coronary occlusion, or heart failure.
Hormone-secreting tumors	Pheochromocytoma, thyroid adenoma or carcinoma, parathyroid adenoma, corticotropin-producing tumors, and insulinoma.
Anxiety-producing drugs	Corticosteroids, neuroleptics used as antiemetics, thyroxine, bronchodilators, beta-adrenergic stimulants,

	antihistamines, and benzodiazepines (paradoxical reactions are often seen in older persons).
Anxiety-producing conditions	Substance withdrawal (from alcohol, opioids, or sedative-hypnotics).
^a Adapted from Massie.[13]	

Patients in severe pain are anxious and agitated, and anxiety can potentiate pain. To adequately manage pain, the patient's anxiety must be treated.[14,15]

Acute onset of anxiety may be a precursor of a change in the metabolic state or of another impending medical event, such as myocardial infarction, infection, or pneumonia. Sepsis and electrolyte abnormalities can also cause anxiety symptoms. Sudden anxiety with chest pain or respiratory distress may suggest a pulmonary embolism. Patients who are hypoxic can experience anxiety; they may fear that they are suffocating.

Many drugs can precipitate anxiety in persons who are ill. For example, corticosteroids can produce motor restlessness, agitation, and mania as well as depression and thoughts of suicide. Bronchodilators and B-adrenergic receptor stimulants used for chronic respiratory conditions can cause anxiety, irritability, and tremulousness. Akathisia, or motor restlessness accompanied by subjective feelings of distress, is a side effect of neuroleptic drugs, which are commonly used for control of emesis. Withdrawal from opioids, benzodiazepines, barbiturates, nicotine, and alcohol can result in anxiety, agitation, and behaviors that may be problematic for the patient who is in active treatment.

Certain tumor sites can produce symptoms that resemble anxiety disorders. Pheochromocytomas and pituitary microadenomas can present as episodes of panic and anxiety.[16] Non-hormone-secreting pancreatic cancers can cause anxiety symptoms. Primary lung tumors and lung metastases can often cause shortness of breath, which can lead to anxiety.

Primary Anxiety Disorders

Patients who have the following symptoms may be experiencing a specific anxiety disorder that was present before they became ill with cancer and that recurs because of the stress of the diagnosis and treatment:

- Intense fear.
- Inability to absorb information.
- Inability to cooperate with medical procedures.

Somatic symptoms include the following:

- Shortness of breath.
- Sweating.
- Lightheadedness.
- Palpitations.

Patients with cancer can present with any of multiple anxiety disorders diagnosed via the criteria of the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5), including:

- Phobias.
- Panic disorder.
- Generalized anxiety disorder.
- Obsessive-compulsive disorder (potentially in the form of obsessiveness about cancer recurrence).
- Health anxiety disorder.
- Post-traumatic stress disorder (if related to cancer diagnosis; refer to the PDQ summary on [Cancer-Related Post-traumatic Stress](#) for more information).
- Anxiety disorder that is caused by another medical condition.

Patients with these anxiety disorders are generally distressed about their symptoms and are usually compliant with behavioral and psychopharmacologic intervention.[5]

Phobias

Phobias are persistent fears or avoidance of a circumscribed object or situation. People with phobias usually experience intense anxiety and avoid potentially frightening situations. Phobias are experienced by cancer patients in a number of ways, such as fear of witnessing blood or tissue injury (also known as needle phobia) or claustrophobia (for example, during a magnetic resonance imaging scan). Phobias can complicate medical procedures and can result in the refusal of necessary medical intervention or tests.[5] Phobias generally respond well to exposure therapy and cognitive behavioral therapy (CBT).

Panic disorder

In panic disorder, intense, rapid-onset anxiety is the predominant symptom, virtually always accompanied by severe somatic symptoms that may include the following:

- Shortness of breath.
- Dizziness.
- Palpitations.
- Nausea.

- Fears of going crazy or that a heart attack is occurring.

Panic disorder is characterized by discrete panic *attacks* that are experienced as happening suddenly, often without a specific trigger, and become intense very quickly. Attacks are self-limiting and generally last for 10 to 20 minutes, though the psychological discomfort and fear of recurrence may last longer. Patients with panic attacks often present with symptoms that can be difficult to differentiate from other medical disorders, though a known history of panic disorder can help clarify the diagnosis. Panic disorder in patients with cancer is most often managed with benzodiazepines and antidepressant medications [5] but also responds well to CBT.

Generalized anxiety disorder

Generalized anxiety disorder is characterized by ongoing, unrealistic, and excessive anxiety and worry about two or more life circumstances, to a degree that is pervasive and does not respond to either reassurance or contrary evidence. The following physical symptoms may be reported but do not have the sudden onset or intensity of panic attacks:

- Motor tension (restlessness, muscle tension, and being easily fatigued).
- Autonomic hyperactivity (shortness of breath, heart palpitations, sweating, and dizziness).
- Vigilance in scanning (feeling keyed up and on edge, irritability, and having exaggerated startle responses).

Obsessive-compulsive disorder

Obsessive-compulsive disorder (OCD) is characterized by persistent thoughts, ideas, or images (obsessions) and by repetitive, purposeful, and intentional behaviors (compulsions) that a person performs to manage his or her intense distress. To qualify as OCD, the obsessive thoughts and compulsive behaviors must be time-consuming and sufficiently distracting to interfere with the person's ability to function in employment, academic, or social situations.

Patients with cancer who have a history of OCD may engage in compulsive behaviors such as hand washing, checking, or counting to such an extent that they cannot comply with treatment. For such patients, normal worry about the cancer diagnosis and prognosis can develop into full obsessive-compulsive symptoms and be severely disabling. OCD is most often managed with serotonergic antidepressant medications (selective serotonin reuptake inhibitors [SSRIs] and clomipramine) and CBT. Milder obsessive thoughts or use of rituals that are not interfering might be addressed with CBT, but medications are not indicated. This disorder is rare in cancer patients who do not have a premorbid history of some type of anxiety disorder.

Health anxiety disorder

Cancer survivors have been known to develop health anxiety disorder related to their fears of recurrence, including hypervigilance to potential physical symptoms; somatization; extreme focus on cancer status; identification with the patient role in care settings; and requesting frequent care, even after high-

maintenance care needs have ended (including, but not limited to, requests for additional office visits and premature maintenance scans).[17] Although research is still ongoing, early clinical guidelines suggest that CBT and treatment with SSRIs may be beneficial.

Screening and Assessment

Effective management of anxiety disorders begins with a thorough and comprehensive assessment and an accurate diagnosis. The normal fears and uncertainties associated with cancer are often intense. Frequently not clear is the distinction between normal fears and fears that are more severe and reach the criteria for an anxiety disorder (refer to [Table 3](#) for more information).[13]

Treatment considerations should take into account the patient's quality of life and not be based solely on the disorder. To assess the severity of the anxiety, it is important to understand how much the symptoms of anxiety are interfering with activities of daily living. Screening for anxiety could include a brief self-report questionnaire that, if a defined cutoff score is exceeded, could then be followed by a more-thorough clinical interview. A variety of general screening questionnaires have been used to identify distress. (Refer to the [Self-Report Screening Instruments](#) section of this summary for more information.) Other anxiety-specific self-report questionnaires (e.g., State-Trait Anxiety Inventory) have also been used, and a questionnaire for the assessment of prostate cancer-related anxiety has been developed and validated.[2,18,19]

The following is a list of symptoms designed to distinguish common or normal worry from more-serious symptoms of anxiety. When patients are reporting the more-serious symptoms, referral to a qualified mental health professional may be warranted.

Table 3. Common Worry versus Anxiety Disorders^a

Symptoms of Common or Normal Worry	More-Serious Symptoms of Anxiety Disorders
Worry comes and goes.	Worry seems constant.
Has some difficulty in concentrating.	Is unable to concentrate.
Is able to "turn off thoughts" most of the time.	Is unable to "turn off thoughts" most of the time.
Has occasional trouble falling asleep.	Has trouble falling asleep and/or wakes up early most nights.

Has occasional crying spells that seem to provide some relief.	Has frequent crying spells that interfere with daily activities.
Fear and apprehension are clearly connected to some upcoming event (e.g., start of treatment, doctor's appointment, or receipt of test results).	Fear and apprehension are more "free floating" and seem to be present most of the time.
Has few, if any, physical symptoms (e.g., racing heart, dry mouth, shaky hands, or restlessness).	Has many physical symptoms (e.g., racing heart, dry mouth, shaky hands, restlessness, fidgetiness, or feeling keyed up).
Has ways to reduce anxiety (e.g., distraction by staying busy).	Has few, if any, ways to reduce anxiety.
^a Adapted from Nicholas.[20]	

Interventions

When anxiety is situational (i.e., produced by pain, another underlying medical condition, a hormone-secreting tumor, or a side effect of medication), the prompt treatment of the cause usually leads to immediate control of the symptoms.[1]

Initial management of anxiety includes providing adequate information and support to the patient. Initial symptoms, which may warrant a psychiatric or psychological consultation, may first be reported to the primary oncologist or surgeon.[21][Level of evidence: IV]

Psychosocial interventions

Psychological approaches include combinations of cognitive behavioral therapy (CBT) techniques, insight-oriented psychotherapy, crisis intervention, couple and family therapy, group therapy, self-help groups,[22] and relaxation-based interventions. These approaches (hypnosis, meditation, progressive relaxation, guided imagery, and biofeedback) can be used to treat anxiety symptoms that are associated with painful procedures, pain syndromes, crisis situations, anticipatory fears, and depressive syndromes.

Combining different approaches can be beneficial for some patients. (Refer to the [Psychosocial Interventions for Distress](#) section of this summary for more information.) Referring patients who may be struggling with anxiety disorders for full assessment and psychological treatment will enhance participation in care, improve quality of life, and reduce the pain experience.[23,24]

One study of 509 recurrence-free breast cancer survivors at 5 to 9 years posttreatment examined the usefulness of a comprehensive intervention that combined positive coping strategies based on CBT (e.g., calming self-talk or relaxation) with education about the disease, treatment, and potential side effects.[25] Findings from this study indicate that women in the intervention group (n = 244) regularly used the intervention components to deal with triggers of fears of breast cancer recurrence and long-term treatment side effects. Most women in the intervention group found the strategies very helpful.[25][Level of evidence: I]

Preliminary evidence suggests racial differences in the use and benefit of specific coping strategies (e.g., religious coping strategies, such as prayer and hopefulness, are used more by African American women and provide greater benefit for these women).[25][Level of evidence: I];[26][Level of evidence: II]

Pharmacologic interventions

Patients with cancer often have symptoms of both anxiety and depression that are caused by stressors related to cancer treatment. Such symptoms of distress often are resolved with psychologic support alone. However, in some cases, pharmacologic interventions are required to address these symptoms. (Refer to [Table 3](#) for descriptions of symptoms of anxiety disorders possibly requiring pharmacological treatment.)

Following are brief descriptions of pharmacological treatment options and potential indications for their use. These descriptions are based on evidence derived from studies conducted in patients without cancer because of the lack of such studies in patients with cancer. However, clinicians have used some of these medications for several decades to treat anxiety symptoms in patients with cancer. The treatment options and their use in the situations described below are also based on clinical experience with these agents in patients with cancer.

The use of medications to treat anxiety disorders is considered when patients are experiencing more-severe symptoms or when their responses to psychosocial interventions are inadequate. When counseling resources are not available or are declined by the patient, medication may be considered sooner rather than later. In certain cases, medications are started simultaneously with psychosocial interventions when it is likely that psychosocial support alone will be inadequate to provide relief or to provide it soon enough.

Pharmacological interventions can be used short-term or long-term, depending on individual patient and illness factors, including the following:

- Severity of anxiety symptoms.
- Level of functional/social impairment.
- Psychiatric history.
- Continued presence of cancer.
- Cancer treatment-related factors contributing to anxiety directly or indirectly (e.g., high-intensity or long-term cancer treatments or treatment with agents known to cause psychiatric symptoms [e.g., cytokines]).

Specific anxiety medications—i.e., medications from the benzodiazepine class, as listed in [Table 4](#)—are frequently used alone or in combination with psychological approaches to provide relief from anxiety symptoms. These medications are effective in the acute treatment of anxiety disorders because of their rapid onset of action. They are frequently used as monotherapy or as adjunctive agents in the short-term management (<4 months) of anxiety disorders. Their long-term use (>4 months) is limited by the potential for abuse and dependence and by their lack of antidepressant effects, as depression is often comorbid with anxiety disorders. Following are some of the indications and safety considerations for the use of benzodiazepines in patients with cancer:[27,28]

- Short-acting benzodiazepines, such as alprazolam and lorazepam, can be effectively used to provide short-term relief at specific points in the cancer continuum of diagnosis, treatment, and recurrence. Examples of such short-term use include the treatment of anxiety during diagnostic procedures (e.g., certain radioimaging procedures) and the treatment of patient anxiety about pending test results (e.g., for yearly mammograms in patients with histories of breast cancer).
- Cancer treatments, such as intensive chemotherapeutic regimens, can cause significant physical and emotional distress and thus exacerbate anxiety. Short-acting or intermediate-acting agents (e.g., clonazepam) can provide significant relief of anxiety and other symptoms (e.g., insomnia secondary to anxiety) during active cancer treatments.
- Longer-acting medications (e.g., diazepam and clorazepate) should generally be avoided because of their long half-lives. These medications can cause or exacerbate cognitive impairment, disorientation, and drowsiness because of their potential for accumulation.
- Patients with medical conditions such as delirium can present with anxiety and agitation. Benzodiazepine use in patients with such conditions is contraindicated because these agents can cause or exacerbate confusion and disorientation.
- All patients, especially elderly patients, receiving benzodiazepines should be closely monitored for cognitive impairment, daytime sedation, and fall risks. Use of these agents should be optimized in elderly patients, patients with multiple comorbidities, patients with liver disease, and patients receiving multiple medications.
- Use of these agents should be closely monitored and optimized in patients receiving other sedating medications, central nervous system depressants, and agents with potential for causing respiratory depression (e.g., opiates).
- It is important to continuously monitor and reevaluate anxiety symptoms in all patients receiving benzodiazepines. Use of these medications can be tapered off if anxiety symptoms resolve with the conclusion of cancer treatments.
- In some patients, the use of benzodiazepines is continued (as monotherapy or as adjunctive treatment) over a longer period (>4 months) because of persistent and debilitating anxiety symptoms. It is important to monitor the development of tolerance, abuse, and dependence issues as well as comorbid depressive symptoms in such patients. Long-term and sometimes chronic use of these agents might be

indicated in a subpopulation of patients, with close monitoring and frequent risk-benefit assessments. Persistent (after 3 or 4 months) anxiety symptoms frequently lead to depression. Patients with persistent anxiety symptoms with or without depression might benefit from alternative treatments (e.g., paroxetine, sertraline).

Table 4. Pharmaceutical Treatments for Anxiety in Cancer Patients^a

Benzodiazepines	• Use acutely, then taper off as tolerated.		
Drug^b	Starting Dose (Range)	Comment(s)	Reference(s)
Alprazolam	0.25–0.5 mg tid (≤4 mg/d)	Available in sustained-release form.	[31][Level of evidence: I]
Chlordiazepoxide	5–10 mg tid–qid	No maximum dose listed.	[31][Level of evidence: I]
		Titrate carefully >40 mg/d.	
Clonazepam	0.125–0.25 mg bid–tid (≤4 mg/d)	More commonly used.	[31][Level of evidence: II]
Clorazepate	30 mg/d in 2–3 doses (≤60 mg/d)		[31][Level of evidence: I]
Diazepam	2–10 mg bid–qid	No maximum dose listed.	[31][Level of evidence: I]
		Titrate carefully >40 mg/d.	

Lorazepam	0.5–1 mg bid–tid (≤10 mg/d)	Preferred in liver disease.	[31][Level of evidence: I]
		More commonly used.	
Oxazepam	10–15 mg tid–qid	No maximum dose listed.	[31][Level of evidence: I]
		Titrate carefully >120 mg/d.	
		Preferred in liver disease.	
Antidepressants	• Use if long-term therapy is needed.		
	• Use with caution with tamoxifen because of CYP2D6 interactions.		
<i>Drug^b</i>	<i>Starting Dose (Range)</i>	<i>Comment(s)</i>	<i>Reference</i>
Citalopram	10–40 mg/d	QTc prolongation.	[31][Level of evidence: II]
		Preferred with tamoxifen.	
Desipramine	25–200 mg/d	Use with caution in elderly patients.	[31][Level of evidence: III]
Duloxetine	20–60 mg/d		[31][Level of evidence: I]
Escitalopram	5–20 mg/d	QTc prolongation.	[31][Level of evidence: I]

		Preferred with tamoxifen.	II]
Fluoxetine	10–60 mg/d	Do not use with tamoxifen.	[31][Level of evidence: II]
Imipramine	10–200 mg/d	Use with caution in elderly patients.	[31][Level of evidence: III]
Mirtazapine	7.5–45 mg/d		[31][Level of evidence: III]
Paroxetine	10–40 mg/d	Do not use with tamoxifen.	[31][Level of evidence: I]
Sertraline	25–200 mg/d		[31][Level of evidence: I]
Venlafaxine	37.5–225 mg/d		[31][Level of evidence: I]
Other Drugs			
<i>Drug^b</i>	<i>Starting Dose (Range)</i>	<i>Comment(s)</i>	<i>Reference</i>
Bupirone	7.5 mg bid	≤30 mg/d for anxiety.	[31][Level of evidence: I]
Hydroxyzine	50–100 mg qid		[31][Level of evidence: I]
Antipsychotics	• Consider for treatment-refractory anxiety.		

		<ul style="list-style-type: none"> • Most associated with significant weight gain. 	
		<ul style="list-style-type: none"> • Also evaluate for metabolic syndrome, and cardiovascular and cerebrovascular side effects. 	
		<ul style="list-style-type: none"> • Risk of QTc prolongation and extrapyramidal side effects. 	
<i>Drug^b</i>	<i>Starting Dose (Range)</i>	<i>Comment(s)</i>	<i>Reference</i>
Aripiprazole	2–10 mg/d	Titrate carefully >15 mg/d.	[31][Level of evidence: II]
Haloperidol	0.5–2 mg bid–tid		[31][Level of evidence: II]
Olanzapine	2.5–10 mg/d		[31][Level of evidence: II]
Quetiapine	12.5–25 mg/d	May titrate >300 mg/d.	[31][Level of evidence: I]
		Benefit seen in some trials.	
Risperidone	0.5–1 mg qd–bid	Titrate carefully >2 mg/d.	[31][Level of evidence: I]

bid = twice a day; CYP = cytochrome P450 enzyme; qd = once a day; qid = 4 times a day; tid = 3 times a day.

^aAdapted from Lorenz et al.,[29] Traeger et al.,[30] and Lexicomp.[31]

^bRefer to the PDQ summary on [Depression](#) for dosing information for antidepressants used to treat anxiety as described in this summary.

The choice of a benzodiazepine depends on the following:

- Duration of action that is best suited to the patient.
- Desired rapidity of onset needed.
- Route of administration available.
- Presence or absence of active metabolites.
- Metabolic problems.

Dosing schedules depend on patient tolerance and require individual titration. The shorter-acting benzodiazepines (alprazolam and lorazepam) are given 3 to 4 times per day. Short-acting benzodiazepines, particularly those that can be administered by multiple routes (lorazepam and diazepam), are effective for high levels of distress. Benzodiazepines decrease daytime anxiety and reduce insomnia. (Refer to the PDQ summary on [Sleep Disorders](#) for more information.) The most common side effects of benzodiazepines are dose dependent and are controlled by titrating the dose to avoid drowsiness, confusion, motor incoordination, and sedation.

All benzodiazepines can cause some degree of respiratory depression, which is generally minimal in patients who have not used benzodiazepines in the past. Benzodiazepines should be used cautiously (or not at all) in cases of respiratory impairment.

Standard precautions should be considered when any sedative drug is used in patients who have borderline respiratory function. Ongoing assessment of this population is important. Low doses of the antihistamine hydroxyzine (25 mg, 2–3 times a day) can be used safely in such situations. In patients with hepatic dysfunction, it is best to use short-acting benzodiazepines that are metabolized primarily by conjugation and excreted by the kidneys (e.g., oxazepam, temazepam, or lorazepam). Another advantage of using lorazepam is its lack of active metabolites. Conversely, other benzodiazepines should be selected in cases of renal dysfunction.

SSRIs (e.g., fluoxetine and sertraline) and serotonin-norepinephrine reuptake inhibitors (SNRIs) (e.g., venlafaxine) are considered first-line pharmacotherapy for long-term management of anxiety disorders. SSRIs and SNRIs are also effective in the treatment of depressive symptoms frequently comorbid with persistent anxiety disorders. SSRIs and SNRIs can take approximately 4 to 6 weeks to take effect because of their slow onset of action. Benzodiazepines are frequently used as adjunctive agents to stabilize symptoms in the initial period of treatment with SSRIs and SNRIs.

Atypical antidepressants (e.g., mirtazapine) are sometimes used to treat anxiety disorders because of their added effects on comorbid symptoms, such as insomnia. Older medications, such as tricyclic antidepressants (e.g., imipramine and clomipramine) and monoamine oxidase inhibitors (e.g., phenelzine), are also effective in treating anxiety disorders. The use of antidepressants in clinical practice is limited by their unfavorable side effects, poorer tolerability, and higher risks of toxicity.^[32]

(Refer to the [Suicide Risk in Cancer Patients](#) section in the PDQ summary on [Depression](#) for more information about the risk of suicidality and other neuropsychiatric side effects.)

Bupirone, a nonbenzodiazepine, is useful in patients who have not previously been treated with a benzodiazepine and in those who may abuse benzodiazepines (e.g., those with a history of illicit substance abuse or alcoholism). Bupirone is also useful in the geriatric population to augment fluoxetine for the treatment of anxiety and depression. The beginning dose is 5 mg 3 times a day and can be increased to 15 mg 3 times a day. Bupirone can also be given twice a day.

The use of specific classes of medications is considered for managing treatment-refractory anxiety symptoms or in certain special clinical situations. Low-dose neuroleptics (e.g., thioridazine, 10 mg 3 times a day; and risperidone, 1 mg twice a day) are used to treat severe anxiety when an adequate dose of a benzodiazepine is ineffective or if the patient might be expected to respond poorly to benzodiazepines (e.g., patients with brain metastases). Low-dose neuroleptics can also be used when benzodiazepines are not helpful or when there is the possibility of delirium, dementia, or other complications. Low-dose anticonvulsants (e.g., pregabalin, 200 mg per day) are sometimes used to treat severe treatment-resistant anxiety when other medications are ineffective or contraindicated because of certain associated risks.[32] Generally, the use of neuroleptics or anticonvulsants is considered after adequate trials with several first-line agents (e.g., SSRIs, SNRIs, and benzodiazepines) because of the significant side effect burden and potential for drug-drug interactions with these agents. Consultation with a psychiatric clinician is strongly recommended before these medications are used. Direct involvement of a psychiatric clinician is imperative for the management of patients receiving these medications.

The presence or absence of specific psychiatric or medical comorbidities is frequently a critical factor in the selection of pharmacological treatments. Pharmacokinetic and pharmacodynamic interactions with other medications are also important factors to be considered in the selection of agents. Following are some examples of such factors and clinical situations driving the selection of pharmacological treatments:

- When depressive symptoms are comorbid with anxiety, treatment with SSRIs, SNRIs, or other antidepressants is strongly considered.
- When neuropathic pain is comorbid with anxiety symptoms, specific antidepressants with known efficacy in treating neuropathic pain (e.g., duloxetine and venlafaxine) are considered.
- When hot flashes are comorbid with anxiety symptoms, specific agents with known efficacy in treating hot flashes (e.g., venlafaxine) are considered.
- Specific medications with known side effects (e.g., nausea with duloxetine or risk of sedation with mirtazapine) are avoided when patients are already experiencing these side effects from their cancer treatments and because of the possible exacerbation of these side effects.
- Patients who are treated with CYP2D6 inhibitors (e.g., paroxetine) and tamoxifen may be at risk of significant drug-drug interactions. (Refer to the PDQ summary on [Hot Flashes and Night Sweats](#) for more information.)

No pharmacological treatment studies have been conducted in children and adolescents with cancer. Furthermore, evidence on pharmacological treatment of anxiety disorders in pediatric patients without cancer is also limited. One meta-analysis of pediatric antidepressant clinical trials [33][[Level of evidence: I](#)] found antidepressants efficacious relative to placebo in the treatment of anxiety disorders, with strongest effects in non-OCD anxiety disorders (e.g., generalized anxiety disorder or social anxiety disorder) and intermediate effects in OCD. (Refer to the PDQ summary on [Depression](#) for a discussion of the risk of suicidal ideation/suicide attempt associated with antidepressant use.)

In general, patients with cancer need to be encouraged to take enough medication to relieve anxiety. Medications are readily tapered and discontinued when symptoms subside. Concerns about addiction are exaggerated in patients with cancer and often interfere with adequate symptom relief.

Current Clinical Trials

Use our [advanced clinical trial search](#) to find NCI-supported cancer clinical trials that are now enrolling patients. The search can be narrowed by location of the trial, type of treatment, name of the drug, and other criteria. [General information](#) about clinical trials is also available.

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Changes to This Summary (03/06/2019)

The PDQ cancer information summaries are reviewed regularly and updated as new information becomes available. This section describes the latest changes made to this summary as of the date above.

Overview

Updated National Comprehensive Cancer Network (NCCN) as [reference 5](#).

Definitions

Updated NCCN as [reference 4](#).

Screening and Assessment

Updated NCCN as [reference 9](#).

Normal Adjustment

Added [fatigue](#) as a symptom experienced by cancer patients that is subthreshold or not severe enough to meet diagnostic criteria.

Added [text](#) about the Better Exercise Adherence after Treatment for Cancer (BEAT Cancer) physical activity behavior change intervention (cited Rogers et al. as reference 36).

Psychosocial Distress

Updated NCCN as [reference 1](#).

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About This PDQ Summary

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