

The Management of Psychological Issues in Oncology

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Abstract: Psychological issues in the cancer setting are highly prevalent and well documented, and can lead to adverse outcomes. Several series of guidelines have been put forth to ensure that both psychological and psychiatric issues are addressed. The management of psychological issues in cancer is relevant for clinicians whose patients are identified clinically or via screening mechanisms with psychological or psychiatric sequelae from cancer. This review describes the psychological impact of cancer, distress screening as a triage mechanism, and the presentation and management of several specific comorbid psychological/psychiatric diagnoses in the oncology setting.

Background

The management of patients with cancer must encompass their psychological well-being.¹ Patients and their families may experience recurrent emotional turmoil in the setting of cancer. Patients come to the cancer diagnosis with varying abilities to cope with stressors. Their psychological experiences in response to cancer and its treatment may be predictable or unpredictable, with varying levels of psychological vulnerability.²

The majority of psychological issues in cancer appear insidiously, and may be normalized by healthcare professionals. Therefore, they frequently are not recognized or treated in a timely fashion,^{3,4} despite the fact that psychiatric disorders are now recognized to occur in approximately 30% to 60% of patients who are newly diagnosed with various types of cancer.⁵⁻⁷ Untreated depression in cancer has been shown to have multiple adverse outcomes. In addition to the mental suffering that it imposes, depression has major effects on morbidity and possibly mortality in cancer.⁸ Evidence suggests that addressing psychosocial, emotional, and physical symptoms early in the cancer trajectory, through such steps as palliative care or psychological interventions, may influence survival outcomes.⁹⁻¹² Comorbid depression with cancer leads to worsened quality of life, increased sensitivity to pain, difficulties with treatment, communication difficulties, caregiver burnout, increased risk of suicide, longer periods of hospitalization, and a reduced expectation of survival.^{8,13-16}

Keywords

Anxiety, cancer, depression, oncology, psychological issues

The Psychological Impact of Cancer

The experience of cancer requires a psychological adjustment. For the most part, people are adaptable and adjust in their own way—one that minimizes the existential threat and can be psychologically healthy. Many people who have successfully navigated a new cancer diagnosis describe the establishment of a “new normal.” Patients with less pronounced coping skills may experience prolonged dysphoric mood, anxiety, appetite changes, insomnia, or irritability that lasts for a variable amount of time. The psychological adjustment may relate to 3 main factors: (1) medical factors, (2) patient-related factors, and (3) societal and cultural factors.¹⁷ Understanding these factors enables general physicians, oncologists, and oncology nurses to better evaluate the patient and suggest more customized recommendations for support. The vast majority of psychological issues occur in reaction to the acute psychological and physical stressors that the cancer diagnosis and its treatment impose on patients. However, antecedent psychological issues and poor coping strategies usually are compounded in the setting of a new cancer diagnosis and its treatment.

Psychological disturbances may present at any time during the cancer trajectory but tend to occur with increased frequency at certain points: at diagnosis, with cancer recurrence or progression, during advanced cancer states, and even after successful treatment.^{18,19} Barriers to the diagnosis of these disturbances include inadequate training or interview skills, a low index of suspicion or awareness of common mental health complications of cancer, and a perceived lack of time.⁵ Similarly, other potential reasons for not addressing these issues in the cancer setting include the underestimation of the prevalence of depressive symptoms, the expectation that all patients will be depressed (ie, depressive symptoms are normalized), and difficulty with exploring emotional symptoms.^{20,21}

Psychological reactions to cancer should be recognized, assessed for underlying psychiatric morbidity, and treated according to existing guidelines and patient preferences.^{22,23} This effort often requires working collaboratively with psychosocial health experts. The need to integrate psychosocial care into the oncology setting is increasingly being recognized. The recognition and treatment of comorbid distress—and possible depression—in accordance with clinical practice guidelines is required for oncology practice of the highest measure.¹

Distress Screening and Psychological/Psychiatric Diagnoses in the Cancer Context

The implementation of distress screening is now used to capture patients who are at risk for a range of psycholog-

ical complications.^{24,25} It relies on a system with adequate psychosocial resources that will escalate psychological care according to diagnosis and patient need.²⁶ In 1996, the National Comprehensive Cancer Network (NCCN) assembled a multidisciplinary panel to explore ways to integrate psychosocial care into routine treatment.²⁴ It was recognized that distress is present in all patients with cancer, and is acceptable to patients as a nonpsychiatric term. The word *distress* covers the range of responses, from the normal distress of fear, worry, and anxiety to formally defined psychiatric disorders, including depression. It is not an official psychiatric diagnosis but helps in screening to recognize those in need. The Institute of Medicine's 2008 report, “Cancer Care for the Whole Patient: Meeting Psychosocial Health Needs,” issued a policy statement that quality cancer care must integrate psychosocial treatments into routine cancer treatment.²⁷ The International Psycho-Oncology Society and the Union for International Cancer Control have endorsed *distress* as the sixth vital sign, after pain.²⁴ In fact, distress screening has been an important step forward in assuring the integration of psychological care in the oncology setting. Seamless collaborative or integrated management of psychological issues in the context of routine care is the goal.

In the setting of cancer, the line between normal and abnormal psychological reactions is often difficult to draw and has not been sufficiently studied. Sadness and worry are normal distress responses to cancer and can even be helpful for some people who take steps to reduce their anxiety (eg, information seeking, seeking out social supports) or deal with their sadness (eg, taking stock of what is important to them). A validated screening instrument can be helpful to identify at-risk patients, but ultimately an interview is needed to adequately assess the symptoms.²⁸

An adjustment disorder is an emotional reaction to a stressor that is out of proportion to the expected reaction and that produces some level of functional impairment. It is by far the most commonly diagnosed psychiatric disorder in patients with cancer, and it often occurs with anxiety.⁵ An adjustment disorder is the mildest level of psychiatric disorder occurring in relation to the stressor of a diagnosis with cancer or its treatment. The line between normal and abnormal is poorly defined, but must be considered within the patient context of disease.

Anxiety disorders typically predate the cancer diagnosis, and have clear symptom clusters as defined by Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria.⁵ These include generalized anxiety disorder, panic disorder, phobias (eg, needle phobia, claustrophobia) and anxiety disorder due to another medical condition. These disorders require careful medical and psychiatric workup to identify potential etiologic stressors, agents, or medical conditions.

Depressive disorders are the second most common disorder, but cause the most functional impairment.²¹ Depressive disorders include major depression, minor depression, and adjustment disorder with depressive features. Depression, as a symptom, is the most frequent psychological problem found throughout the cancer trajectory, although differences in prevalence occur with sex, age, cancer type, and even the economic aspects of treatment.^{29,30} Depression is more common in patients with pancreatic (33%-50%), oropharyngeal (22%-57%), breast (4.5%-46%) and lung (11%-44%) cancers.³¹ Variations in the criteria used to define and measure depression, along with disparate cancer populations of study (eg, diagnosis and stage, hospitalization status, time since diagnosis) account for the tremendous variability in prevalence.^{32,33} A recent meta-analysis reported a 16.3% prevalence of all types of depressive disorders.⁵ However, the prevalence of depressive symptoms among patients receiving palliative care is 25% to 29%, and the prevalence of a major depressive episode among these patients is 14% to 17%.⁵ The average prevalence of a major depressive episode in cancer populations is 5% to 10%, which is 2 to 3 times higher than in the general population.³⁴

The Treatment of Psychological Issues and Psychiatric Disorders in Oncology

Several models exist for addressing psychological issues in oncology, including (1) the distress screening/triage model, (2) the primary provider (oncologist/nurse)-driven model, and (3) collaborative care models.

The first model assumes that appropriate psychosocial resources are in place and that referrals will be made to appropriate psychosocial oncology professionals according to escalating needs. This model is endorsed by the NCCN.³⁵

The second model is oncology team-driven, and may be enhanced with psychosocial educational interventions to help primary oncology providers. This model assumes that the oncology provider will have some psychosocial expertise to initiate and maintain psychosocial care and understand when referral is necessary.

The third model assumes that psychosocial care will be delivered by the primary oncology team but with enhanced guidance from psychosocial professionals. This review focuses on the treatment of psychological/psychiatric issues by primary oncology providers.

Psychotherapeutic Interventions for Patients With Cancer

Patients highly value their relationships with their oncologic providers, and positive support and encouragement are meaningful interventions.¹ The oncologist can empha-

size the benefits of psychological care as a means to obtain better cancer care. Reframing negative cognitions (ie, correcting erroneous thoughts) and supporting the “ego” function (eg, focusing on what patients are doing well) are effective interventions that provide emotional support.^{36,37}

Although supportive psychotherapy by an oncology or psychosocial oncology professional is the cornerstone of emotional support for patients with cancer, additional psychotherapeutic and psychiatric interventions should be provided depending on the needs of the patient.³⁸ Psychological issues in oncology are myriad. Although the majority of psychological issues in oncology are in response to the psychological stressor of having a life-threatening illness, some psychological/psychiatric issues are biologically induced or result from medications. The outcomes of untreated psychological issues in cancer recently have been identified, and the concurrent treatment of psychological issues in cancer has been shown to improve outcomes.^{11,39}

Cancer-specific issues exist, especially for those patients with breast, prostate, and head/neck cancers, for example, and psychological attention should be directed appropriately across cancer subtypes.⁴⁰ Addressing psychological issues in oncology has been found to lead to improved patient outcomes and improved patient satisfaction with doctor and nurse communication.^{10,41}

Psychological/Psychiatric Management of Patients With Cancer Who Have Specific Disorders

Psychological and psychiatric management of patients with cancer varies depending on the specific disorder, whether that be psychological distress, an adjustment disorder, an anxiety disorder, a depressive disorder, delirium, pain, or fatigue.

Psychological Distress. The management of distress should be problem-focused, directed toward ameliorating the cause of distress if possible, and directed toward symptoms.²⁵ A thorough review of symptoms and medications should address any medical or medication-induced psychological distress. Guidance from specialists to fully assess the effects of a medical or medication-related cause of the patient’s symptoms plays a crucially important role.²⁵ A formal psychiatric diagnosis should be ruled out depending on the safety assessment and severity of symptoms.

The NCCN recommends the Distress Thermometer (DT) and the accompanying Problem List (PL) to screen for distress.³⁵ These tools have been used widely by cancer institutions to meet the Commission on Cancer distress-screening mandate for accreditation in 2015.^{23,42} The DT is a 1-item measure of distress, and the PL can be helpful in identifying causes of distress, along with a

problem-focused clinical interview.³⁵ Referrals should be made to the appropriate clinician in order to obtain a comprehensive assessment. For instance, a social worker may best address financial issues and a chaplain may best address spiritual issues. A standardized tool should be used to screen for distress, such as the DT and PL, the Beck Depression Inventory, or the General Health Questionnaire-28.^{6,43,44}

In general, acknowledging patient distress is the beginning of a therapeutic intervention. Many patients benefit simply from reviewing and clarifying information about their diagnosis, treatment options, and side effects. Patients frequently receive information from various professional and lay sources that runs counter to their understanding. It can be helpful to review how to interpret the information that is gathered in the medical system. Always assess for patient understanding, and refer to appropriate sources (eg, NCCN Guidelines for Patients). Counseling patients on how to mobilize and avail themselves of resources, and ensuring continuity of care, can be highly therapeutic and can help to establish a rapport. Depending on the patient's needs, counseling (eg, support groups, family or individual counseling), symptom-directed interventions (eg, relaxation techniques such as guided imagery, meditation, or creative art/music therapies), spiritual support, or exercise should be provided. In many cases, collateral information and follow-up patient interviews are helpful to assess for the need to escalate care. Repeat evaluations should be provided after any suggested therapeutic interventions.²⁵

Standards for distress management have been developed by the NCCN.³⁵ Distress should be recognized, monitored, documented, and treated promptly at all stages of disease and in all settings.²⁴ The NCCN suggests that interdisciplinary committees review institutional standards for distress management. The training of professionals in distress screening and communication skills is mandatory in order to ensure the proliferation of skill sets.⁴⁵

Adjustment Disorders. Adjustment disorders occur when the patient has symptoms (eg, anxiety, excessive worry, depression, hopelessness, loss of appetite) that exceed what would be expected from the stressor, and a loss of social or occupational function directly related to the cancer stressor.^{46,47} These disorders may be hard to detect in the cancer setting. Situational symptoms generally include insomnia, worry, muscle tension, restlessness, dyspnea, dyspepsia, palpitations, sweating, jitteriness, light-headedness (ie, with anxious features), irritability, mood swings, or transient spells of hopelessness or demoralization (ie, with mixed or depressive features). Tearfulness that is experienced as an emotional release suggests an adjustment disorder; whereas crying with

major depression is more likely to feel emotionally draining and not relieving for the patient.⁴⁶ Transient fixation on cancer-related phenomena (ie, tumor markers or scan fixation) might be indicative of an adjustment disorder.⁴⁸ Adjustment disorders can be acute (ie, lasting <6 months) or chronic (ie, lasting \geq 6 months) in the presence of an ongoing stressor.⁴⁹

Psychotherapy should be considered for all adjustment disorders. Therapy should focus on restoring the patient's ability to cope with stressors and thrive in regular daily activities. It should help ameliorate stressors, if possible. In the cancer setting, clarifying what is a realistic understanding of the seriousness of the diagnosis and prognosis can be hugely beneficial.³⁷ Individual, group, or supportive therapy may focus on adapting to and accepting the diagnosis, adjusting the interpretation, and finding meaning in the experience. Appropriate therapies should be directed toward a reduction of symptoms and should support coping resources. This may be best done by problem solving and by ameliorating symptoms with supportive counseling and/or psychopharmacology. Management should be patient-directed and in accordance with preferences for treatment, but with explicit professional guidance. Also, assessments for safety and to exclude other psychiatric disorders are imperative. Educating patients, controlling physical symptoms, and maintaining effective communication are essential therapeutic tools that restore patients' innate coping abilities.

Patients may benefit from participating in a support group or a supportive-expressive psychotherapy group that is focused on current life problems with other patients.⁵⁰ Supportive-expressive group psychotherapy, based on Luborsky's model of Core Conflictual Relationship Theme, utilizes expressive interventions to enhance the patient's cognitive and emotional understanding of his or her symptoms.⁵¹ A "helping alliance" is created collectively by the therapist and by other group members.⁵² This model has been manualized for a number of psychiatric diagnoses and has been specifically adapted for Spiegel's model of supportive-expressive group therapy for patients with cancer.⁵³ Various interpretations of efficacy have been shown for women with breast cancer, in which the intervention has been particularly well studied.^{11,54,55} Cognitive behavioral therapy (CBT) may be effective for assessing overly negative or irrational interpretations and instituting symptom-directed behavioral interventions for insomnia and fatigue, for example.⁵⁶ Psychological interventions are effective, and their implementation can even be taught to non-mental health professionals in certain cases.^{37,57} This approach may be effective because evidence suggests that cancer patients prefer more support and communication directly from the oncology clinical staff.⁵⁸

Psychotropic medication should be considered for moderate to severe adjustment-type disorders to address symptoms specifically.⁵⁹ For instance, insomnia may be addressed with a hypnotic agent or an anxiolytic agent to reduce worry. If there is no response to medication, dosages should be titrated.⁶⁰ If there is no subsequent response, another disorder with or without a personality disorder should be considered. After a response is achieved, patients should be followed and reassessed, and medication should be de-escalated if no longer needed. Treatment for any mood disorder should always consider the underlying medical etiology of the mood disturbance and should be directed toward ameliorating the specific symptoms that are the most distressing (eg, anhedonia, fatigue, insomnia, anorexia, suicidal thoughts). Restoration of the functional impairment (eg, improved relationships, functioning at work or at home, attending to obligations) may signal treatment response and resolution of the adjustment disorder. Patients who have had functional impairment at one point during the cancer trajectory are at risk for further impairment with escalation of psychological symptoms, and should be monitored carefully.

Anxiety Disorders. Intense fear, an inability to absorb information, and an inability to cooperate with medical requests may be presenting features of an anxiety disorder.⁶¹ Anxiety leads to poor quality of life, independent of its association with depression (it is largely comorbid with depression). Although 34% of patients may have clinical symptoms of anxiety, the majority of anxiety disorders in the cancer setting are a reactivation of a previously diagnosed disorder.¹⁹ Anxiety disorders can detract from patient-centered care because patients may sabotage their involvement in medical decision-making, and may have multiple exacerbations of medical symptoms that lead to excessive work-ups and possibly more invasive tests and disruptions in cancer care. Psychosocial assessment may benefit from multidisciplinary input, and communication should be sought with the primary oncology team and consultants. Palliative care specialists may be able to provide expertise in the management of underlying pain or other physical or spiritual issues. Other specialists may provide insightful management based on their areas of expertise. Also, primary care providers may be able to provide a unique assessment of psychosocial adjustment that may predate the cancer diagnosis.

Symptoms of anxiety typically consist of cognitive, emotional, physical, and behavioral components.⁶¹ Cognitively, patients may fixate their focus on threats (eg, cancer and otherwise), worry excessively, catastrophize, and underestimate their ability to cope. Emotionally, they may feel nervous, panicky, or just plain scared. Physically,

they may feel breathless and experience chest tightness, palpitations, gastrointestinal discomfort (diarrhea/nausea), diaphoresis, and muscle tension. Behaviorally, patients may act in a way that avoids the immediate threat they fear, seek reassurance, or become paralyzed with anxiety.

Each type of anxiety disorder can present with the somatic signs of autonomic hyperreactivity (eg, shortness of breath, sweating, lightheadedness, palpitations), motor tension (eg, restlessness, muscle tension, fatigue), and/or vigilance (eg, irritability, exaggerated startle response, feeling “on edge”).⁶²

The treatment of anxiety disorders in patients with cancer includes a range of pharmacologic, psychosocial, and psycho-educational interventions. The clinical management of anxiety disorders should be directed toward the specifically diagnosed anxiety disorder and is similar to treatment in the general population.

Psychosocial interventions consist of education and psychotherapy (CBT and supportive-expressive therapy), stress management, and supportive counseling.⁵⁴ CBT therapies are goal-oriented and focus on restructuring thinking patterns and behaviors, whereas supportive-expressive therapies offer a nondirective approach that allows patients to process their cancer-related experiences.⁶³ Mind-body approaches may be helpful to ameliorate anxiety symptoms. Patients should be encouraged to utilize other available sources (eg, a chaplain, a local cancer organization).⁶⁴

Pharmacologic interventions in cancer should be guided by the anxiety diagnosis, the side effect profile of the drug, symptom severity, and patient preference.⁶⁵ In panic disorder, antidepressant medications should be started at recommended low doses or even lower to ensure tolerability. Attention should be placed on titrating the psychotropic medication to the desired beneficial effect. Patients should be maintained on antidepressant medication for at least 2 to 4 weeks unless they are not tolerating the side effects. For generalized anxiety disorder, therapeutic trials of anxiolytic medications are not as long because their benefit is seen within a couple of doses. Certain antipsychotic medications (eg, olanzapine) are now more commonly used in oncology settings to alleviate anxiety, chemotherapy-induced nausea, or hiccups. Indications for the use of psychotropic medication in oncology extend beyond mood disorders to cancer-related fatigue, anorexia and weight loss, hot flashes, delirium, sleep disturbances, nausea, and chemotherapy-induced neuropathy.

Unfortunately, there are few data about the relative or additive effects of pharmacology to psychosocial interventions in the cancer setting. A list of commonly used antidepressants and benzodiazepines is provided in the table.

Benzodiazepines may play a useful role in helping

Table. Psychotropic Medications Commonly Used in Oncology

	Dosing (mg/day)	Unique Benefits	Possible Side Effects
SSRI Antidepressants^a			
Fluoxetine	10-80	Minimal risk of discontinuation syndrome owing to long half-life	Nausea, nervousness, weight gain, insomnia, inhibition of tamoxifen metabolism and other CYP2D6 substrates
Sertraline	25-200	Few DDIs	Headache, diarrhea, constipation, sexual dysfunction, restlessness
Paroxetine	5-60	Useful to treat comorbid anxiety	Inhibits conversion of tamoxifen to endoxifen; high potential for DDI via CYP450 enzymes; high discontinuation syndrome owing to short half-life; weight gain, sedation, dry mouth
Citalopram	10-40	Few DDIs	Headache, diarrhea, constipation, sexual dysfunction, restlessness
Escitalopram	10-20	Few DDIs; S-enantiomer of citalopram	Headache, diarrhea, constipation, sexual dysfunction, restlessness
Trazodone	25-400	Sleep aid	Significant sedation; orthostasis, priapism, sexual dysfunction
SNRI Antidepressants			
Venlafaxine	37.5-300	Least likely to interact with tamoxifen; useful for hot flashes, neuropathic pain; few CYP450 interactions	Exacerbates hypertension; significant discontinuation syndrome
Desvenlafaxine	50	Metabolite of venlafaxine	
Duloxetine	20-60	Useful for hot flashes, neuropathic pain	Exacerbation of narrow angle glaucoma; hepatic insufficiency; sedation; urinary retention
Miscellaneous Antidepressants			
Mirtazapine	7.5-45	Stimulates appetite, weight gain; treats nausea; acts as sleep aid at lowest dose (7.5 mg) and as anxiolytic, antidepressant at higher doses	Somnolence, myalgias, weight gain, hyperlipidemia; rare but serious agranulocytosis; CYP1A2, CYP3A4 substrate
Bupropion	300-400	Noradrenergic and dopaminergic; may treat nicotine dependence	Lowers seizure threshold at high doses; strong CYP2D6 inhibitor
Benzodiazepines			
Alprazolam	0.125-2 orally; t _{1/2} , 6-20 h	No cross-tolerance with other benzodiazepines	Significant rebound anxiety; multiple CYP3A4 drug interactions
Clonazepam	0.25-4 orally; t _{1/2} , 20-50 h	Helpful in management of anxiety, seizure disorders, nocturnal sleep disorders, neuralgia, mania; may have less abuse liability than shorter-acting agents	Psychomotor impairment; respiratory depression
Diazepam	1-20 orally, IV, or IM; t _{1/2} , 30-60 h	Helpful in management of anxiety, alcohol withdrawal, muscle spasm, seizure disorders	Psychomotor impairment; respiratory depression; bradycardia

(Table continues on page 1005)

Table. (Continued) Psychotropic Medications Commonly Used in Oncology

	Dosing (mg/day)	Unique Benefits	Possible Side Effects
Benzodiazepines (continued)			
Lorazepam	0.5-2 orally, IV, or IM; $t_{1/2}$, 10-18 h	Antiemetic; alcohol withdrawal; preferable in those with liver disease because not subject to phase 1 metabolism	Psychomotor impairment; respiratory depression; bradycardia
Miscellaneous Anxiolytics			
Gabapentin	900-3600 in daily divided doses, 3× per day	Also treats neuropathic pain; sleep aid; may decrease alcohol cravings	Sedation; renal dosing; myoclonus
Bupirone	20-30 2-3× per day	Nonbenzodiazepine	Avoid use in renal or hepatic impairment; monitor for serotonin syndrome, extra-pyramidal symptoms
Hydroxyzine	200-400 daily divided dose, every 6 h	Nonbenzodiazepine; treats anxiety, nausea, insomnia	Monitor for anticholinergic side effects; renal dosing
Psychostimulants			
Methylphenidate	2.5-40	Quick relief from depressive symptoms, fatigue; effective in medically ill populations and does not usually cause weight loss, unlike in medically healthy populations; available in many dose and duration formulations	Agitation, restlessness, irritability, anorexia; hypertension
Dextroamphetamine	5-60	More potent than methylphenidate; dosed daily	Agitation, restlessness, irritability, anorexia; hypertension
Modafinil	100-200	Nonstimulant; long-lasting	Agitation, irritability; Stevens-Johnson syndrome; CYP3A4 substrate; CYP2C19 inhibitor; major CYP3A4 inducer; cost
Antipsychotics			
Olanzapine	2.5-20	Used as adjunct in treatment-refractory depression; can be used to treat chemotherapy-induced nausea; used to treat mania and as a mood stabilizer in bipolar disorder; used to treat psychotic disorders	QTc prolongation; somnolence; weight gain, metabolic syndrome
Haloperidol	0.5-5	Used to treat agitation/delirium; can be used to treat chemotherapy-induced nausea	QTc prolongation; somnolence; weight gain, metabolic syndrome

CYP, cytochrome; DDIs, drug-drug interactions; h, hours; IM, intramuscularly; IV, intravenously; QTc, corrected QT; SNRIs, serotonin-norepinephrine reuptake inhibitors; SSRIs, selective serotonin reuptake inhibitors.

*SSRI class antidepressants are the drug of choice in these patients. Their efficacy has been established in randomized controlled trials, they have possible anti-inflammatory and cellular effects in cancer, and they generally are well tolerated. They have the potential to cause serotonin syndrome.

the anxious cancer patient. However, all benzodiazepines have the potential side effects of sedation, dizziness, and incoordination, along with the potential for tolerance and abuse or dependence. In particular, the shortest-acting benzodiazepine, alprazolam, can cause rebound anxiety and carries an elevated risk of abuse and dependence. Its use should be limited to specific indications (eg, one-time administration for procedures, to halt a panic attack in panic disorder). All benzodiazepines may cause bradycardia and respiratory depression (particularly diazepam and lorazepam), drug-drug interactions (eg, alprazolam and triazolam), impaired memory and disorientation, and rebound anxiety. They also have the potential to cause withdrawal symptoms. A clear indication and monitoring plan should be prescribed for the patient, and these medications should be reserved for moderate to severe symptoms.

Hypnotics may be prescribed for short-term insomnia after taking a detailed history of sleep hygiene, depression, anxiety, and substance use; and sleep hygiene education, relaxation training, and other nonpharmacologic approaches have been attempted. Hypnotics that act on the gamma-aminobutyric acid (GABA) system are preferred, such as zolpidem or zaleplon.

Most cancer-related anxiety therapies take a generalist approach, but specific anxiety disorders should be managed by more directed approaches. For example, comorbid panic disorder may be treated using systematic desensitization (a type of CBT) and/or medications approved by the US Food and Drug Administration (FDA) for use in depression: fluoxetine, paroxetine, sertraline, and venlafaxine.³⁸

Treatment of generalized anxiety disorder may utilize various psychotherapies and/or the commonly used antidepressants fluoxetine, paroxetine, escitalopram, sertraline, venlafaxine, and duloxetine. Posttraumatic stress syndrome should be treated with the FDA-approved agents sertraline and/or paroxetine.

Oncology teams should utilize appropriate referrals for specialized supportive care (eg, pastoral care, palliative care, social work) when necessary. Psycho-oncologists must have knowledge of psychiatric medication use in oncology, because up to 50% of patients will take a psychiatric medication (eg, anxiolytic, hypnotic, antidepressant) during the course of their illness.^{66,67} Consulting teams may put together a complete psychosocial plan to comprehensively address the patient's problems. Mental health professionals should manage most severe anxiety disorders.

Depressive Disorders

Depressive disorders vary in severity and lead to a spectrum of symptoms and dysfunction. In the cancer setting,

the diagnosis is more difficult because adapting to losses related to illness is difficult to distinguish from depressive symptoms. Understanding the prevalence of depression in cancer is limited by our understanding of depression in general. In the public domain, depression can mean anything from a transient depressed mood to severe psychotic depression leading to suicide. As an illness, it can be conceptualized as either a dimension (eg, a symptom spectrum) or as a category (eg, a disorder). Both conceptualizations are helpful in understanding depression. Specific depression criteria in medically ill patients, such as the Cavanaugh and the Endicott criteria, have been examined and may be helpful for identifying depression in the cancer setting, although they are not frequently used.⁶⁸ In addition, several other barriers exist for diagnosing depression in the cancer context, including the following: the myth that all cancer patients are depressed; difficulty distinguishing between depression and normal sadness; misconception that depression is a normal part of the disease process; and the clinician's fear of fully exploring psychological symptoms at a vulnerable time.⁶⁹

Despite diagnostic ambiguity, depression can be recognized in the cancer setting through clinical interpretation and with the aid of a screening instrument. Even relatively short instruments that screen for distress and depression have proven validity against gold standard measures of depression, eg, the trained clinician.^{43,44,70} For example, the clinician can recognize depression using the Patient Health Questionnaire-2 (PHQ-2) questions, "Over the last 2 weeks, how often have you been bothered by any of the following problems: (1) little interest or pleasure in doing things? (2) feeling down, depressed, or hopeless?" If the patient scores at least 3 out of 6 total points, the Patient Health Questionnaire-9 (PHQ-9) should be used to further delineate the depressive symptoms. The PHQ-9 questions are very similar to DSM-5 criteria for major depression. Suicide risk needs to be assessed whenever a diagnosis of depression is considered. However, no measure offers 100% sensitivity or specificity, and a skilled clinical assessment and interpretation of findings is always required in order to rule out confounding variables and provide adequate depression care.⁷¹

Similar to anxiety disorders, the treatment of depressive disorders in patients with cancer includes a range of pharmacologic, psychosocial, and psycho-educational interventions. Psycho-education, psychotherapy (eg, CBT, supportive-expressive therapy), stress management, and supportive counseling are the cornerstone of supportive care for depression in cancer.⁵⁴ CBT therapies focus on restructuring thinking patterns and behaviors, whereas supportive-expressive therapies allow patients to process their cancer-related experiences.⁶³ Supportive-expressive group psychotherapy has been studied extensively in

women with breast cancer and depression.⁷² An emotional and cognitive understanding of core conflicts is sought through the use of a helping therapeutic alliance. Other adjuvant-type therapies, including hypnosis and relaxation techniques (eg, mindfulness techniques), may help to alleviate concomitant anxiety symptoms.^{73,74} Because depression may severely lessen patients' drive to seek help, patients should be actively encouraged to utilize available sources. The physician should be able to direct the patient toward the most appropriate resources.⁶⁴ Of note, meaning-centered psychotherapy has shown therapeutic efficacy in decreasing fear of recurrence and helping patients face the uncertainties of the cancer experience.⁷⁵ Meaning-centered psychotherapy, whose core tenets are based on Viktor Frankl's logotherapy, has been made specific for patients with cancer. This recently developed therapy is being tested in various settings, and has been found to be efficacious in group settings.⁷⁶

Pharmacologic interventions are guided by the diagnosis, the side effect profile of the drug, symptom severity, and patient preferences.⁶⁵ The patient's therapeutic course with the antidepressant should be monitored closely to ameliorate side effects and offer encouragement. Most medications need to be titrated to effect, which should depend on perceived benefit and tolerability of the medication. A trial of at least 2 to 4 weeks is typical unless the patient is not tolerating the side effects. After that amount of time and subsequent titration, a decision should be made about switching the antidepressant. If a marginal benefit was obtained, an adjuvant medication could be considered. This adjuvant medication might be another antidepressant, typically bupropion or mirtazapine, an antipsychotic such as aripiprazole or olanzapine, or a stimulant such as methylphenidate, depending on symptomatology. Of course, psychiatric medications are used to treat a multitude of symptoms in oncology and should ideally be used to target more than one symptom, such as fatigue, nausea, hot flashes, neuropathy, weight loss, sleep disturbance, anxiety, or even hiccups.

Delirium. Delirium is the most common neuropsychiatric diagnosis among cancer patients and is caused by either the cancer directly or by indirect complications of the disease, cancer treatment, or other medical problems.⁷⁷ It is characterized by an abrupt onset of disturbances in consciousness or arousal.⁷⁸ The hallmark of delirium is the fluctuation in attention, cognition, and perception over the course of a day. Two primary forms exist, hyperactive and hypoactive.⁷⁸ Because hypoactive is the most common form, delirium is frequently under-recognized or misdiagnosed in patients with cancer.⁷⁷ Even when recognized, it is frequently undertreated or inappropriately treated. Older patients and those with

underlying cognitive impairment (eg, dementia) are at increased risk for developing delirium during the course of cancer diagnosis and treatment.⁷⁸

Delirium is often managed by primary teams but with the consultative help of neurology or psychiatry. The standard approach to treating delirium is to search for the underlying causes and correct those factors while managing the symptoms of delirium by using both pharmacologic and nonpharmacologic strategies. The vast majority of delirium stems from an underlying medical condition (eg, infection) or medications, although the cause also can be multifactorial. Therefore, it is most important to address any modifiable risk factors for delirium (eg, polypharmacy, malnutrition, visual impairment, insomnia, or dehydration).

The most important treatment is to correct the underlying medical or medication cause. Antipsychotic medications are helpful and frequently are used to restore the sleep-wake balance or to ameliorate hyperactive symptoms. Antipsychotics, cholinesterase inhibitors, and alpha-2 adrenergic receptor agonists are the main classes of medications studied in the treatment and prevention of delirium. However, no medication to date has been specifically approved by the FDA for treatment or prevention of delirium.^{77,79} The most common antipsychotic medications used to treat delirium are highlighted in the table.

Nonpharmacologic treatment for patients with delirium includes prevention of delirium in the first place. This involves an assessment of modifiable risk factors, including underlying cognitive impairment or disorientation, dehydration, constipation, hypoxia, infection, immobility, polypharmacy, pain, poor nutrition, sensory impairment, and sleep disturbance. Preemptively addressing these factors has been shown to reduce the time that patients are impaired.⁷⁷

Pain. The psychiatric impact of pain in cancer cannot be underestimated.⁸⁰ Patients with uncontrolled pain experience a high prevalence of psychiatric complications that may be ameliorated by adequate pain control.⁸¹ At the same time, psychological factors (eg, anxiety and depression) and the patients' self-ascribed meaning of the pain experience intensify cancer pain.⁸² Desire for hastened death, a psychological entity similar to depression, decreases with better pain management.⁸³ Additionally, geriatric patients may "somatize" with increasingly complicated pain complaints when there is an underlying depressive disorder. Therefore, it is important to recognize any concomitant underlying depressive component of the patients' pain, and to treat both. Pain symptoms often remit with depression treatment. Somatizing may be suspected when pain symptoms do not improve with pain treatments.

Fatigue. Cancer-related fatigue should be addressed by evaluating for other overlapping psychological problems—such as anxiety, depression, pain, and sleep disturbances—that carry a fatigue component. However, cancer-related fatigue is also extremely common on its own. The NCCN practice guidelines for cancer-related fatigue recommend screening for fatigue using a 0 to 10 rating scale, and identifying and treating underlying causes of fatigue if possible.

Nonpharmacologic treatments for fatigue include increasing physical activity, increasing psychosocial support, addressing sleep problems, and addressing any nutritional deficiencies. Although data on fatigue treatments are limited, exercise and cognitive behavioral therapy have been identified as effective treatments against cancer-related fatigue. In addition, psychopharmacologic interventions have been used. Although stimulants are frequently used to treat opioid-induced fatigue, the evidence for their effectiveness in treating cancer-related fatigue is mixed.

Conclusion

The patient experience of cancer requires psychological adaptations that should be assessed, evaluated, and treated as necessary alongside the cancer diagnosis. Distress screening and increased attention to the psychological realm of cancer have contributed to tremendous advances in the realm of psycho-oncology over the past 20 years.

It is imperative for the oncologic clinician to understand the basic concepts and categorization of psychological problems in cancer, and how to initiate treatment. This review on the categorization of psychological/psychiatric disorders in cancer and their management should be helpful for clinicians who seek greater information.

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References

- Wein S, Sulkes A, Stemmer S. The oncologist's role in managing depression, anxiety, and demoralization with advanced cancer. *Cancer J*. 2010;16(5):493-499.
- McFarland DC, Andreotti C, Harris K, Mandeli J, Tiersten A, Holland J. Early childhood adversity and its associations with anxiety, depression, and distress in women with breast cancer. *Psychosomatics*. 2016;57(2):174-184.
- Fallowfield L, Ratcliffe D, Jenkins V, Saul J. Psychiatric morbidity and its recognition by doctors in patients with cancer. *Br J Cancer*. 2001;84(8):1011-1015.
- Fallowfield L, Jenkins V. Psychosocial/survivorship issues in breast cancer: are we doing better? *J Natl Cancer Inst*. 2014;107(1):335.
- Mitchell AJ, Chan M, Bhatti H, et al. Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies. *Lancet Oncol*. 2011;12(2):160-174.
- Mitchell AJ. Pooled results from 38 analyses of the accuracy of distress thermometer and other ultra-short methods of detecting cancer-related mood disorders. *J Clin Oncol*. 2007;25(29):4670-4681.
- Mehnert A, Brähler E, Faller H, et al. Four-week prevalence of mental disorders in patients with cancer across major tumor entities. *J Clin Oncol*. 2014;32(31):3540-3546.
- Satin JR, Linden W, Phillips MJ. Depression as a predictor of disease progression and mortality in cancer patients: a meta-analysis. *Cancer*. 2009;115(22):5349-5361.
- Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med*. 2010;363(8):733-742.
- Bakitas MA, Tosteson TD, Li Z, et al. Early versus delayed initiation of concurrent palliative oncology care: patient outcomes in the ENABLE III randomized controlled trial. *J Clin Oncol*. 2015;33(13):1438-1445.
- Giese-Davis J, Collie K, Rancourt KM, Neri E, Kraemer HC, Spiegel D. Decrease in depression symptoms is associated with longer survival in patients with metastatic breast cancer: a secondary analysis. *J Clin Oncol*. 2011;29(4):413-420.
- Spiegel D, Giese-Davis J. Depression and cancer: mechanisms and disease progression. *Biol Psychiatry*. 2003;54(3):269-282.
- Skarstein J, Aass N, Fosså SD, Skovlund E, Dahl AA. Anxiety and depression in cancer patients: relation between the Hospital Anxiety and Depression Scale and the European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire. *J Psychosom Res*. 2000;49(1):27-34.
- Prieto JM, Blanch J, Atala J, et al. Psychiatric morbidity and impact on hospital length of stay among hematologic cancer patients receiving stem-cell transplantation. *J Clin Oncol*. 2002;20(7):1907-1917.
- Misono S, Weiss NS, Fann JR, Redman M, Yueh B. Incidence of suicide in persons with cancer. *J Clin Oncol*. 2008;26(29):4731-4738.
- Colleoni M, Mandalà M, Peruzzotti G, Robertson C, Bredart A, Goldhirsch A. Depression and degree of acceptance of adjuvant cytotoxic drugs. *Lancet*. 2000;356(9238):1326-1327.
- Mehta RD, Roth AJ. Psychiatric considerations in the oncology setting. *CA Cancer J Clin*. 2015;65(4):300-314.
- Delgado-Guay M, Parsons HA, Li Z, Palmer JL, Bruera E. Symptom distress in advanced cancer patients with anxiety and depression in the palliative care setting. *Support Care Cancer*. 2009;17(5):573-579.
- Kangas M, Henry JL, Bryant RA. The course of psychological disorders in the 1st year after cancer diagnosis. *J Consult Clin Psychol*. 2005;73(4):763-768.
- Fann JR, Thomas-Rich AM, Katon WJ, et al. Major depression after breast cancer: a review of epidemiology and treatment. *Gen Hosp Psychiatry*. 2008;30(2):112-126.
- Chochinov HM. Depression in cancer patients. *Lancet Oncol*. 2001;2(8):499-505.
- Andersen BL, DeRubeis RJ, Berman BS, et al; American Society of Clinical Oncology. Screening, assessment, and care of anxiety and depressive symptoms in adults with cancer: an American Society of Clinical Oncology guideline adaptation. *J Clin Oncol*. 2014;32(15):1605-1619.
- Pirl WF, Fann JR, Greer JA, et al. Recommendations for the implementation of distress screening programs in cancer centers: report from the American Psychosocial Oncology Society (APOS), Association of Oncology Social Work (AOSW), and Oncology Nursing Society (ONS) joint task force. *Cancer*. 2014;120(19):2946-2954.
- Holland JC, Bultz BD; National Comprehensive Cancer Network (NCCN). The NCCN guideline for distress management: a case for making distress the sixth vital sign. *J Natl Compr Canc Netw*. 2007;5(1):3-7.
- Holland JC, Andersen B, Breitbart WS, et al. Distress management. *J Natl Compr Canc Netw*. 2013;11(2):190-209.
- Carlson LE, Waller A, Mitchell AJ. Screening for distress and unmet needs in patients with cancer: review and recommendations. *J Clin Oncol*. 2012;30(11):1160-1177.
- Adler NE, Page AE, eds. *Cancer Care for the Whole Patient: Meeting Psychosocial Health Needs*. Washington, DC: National Academies Press; 2008.
- Wagner LI, Spiegel D, Pearman T. Using the science of psychosocial care to implement the new American college of surgeons commission on cancer distress screening standard. *J Natl Compr Canc Netw*. 2013;11(2):214-221.
- van't Spijker A, Trijsburg RW, Duivenvoorden HJ. Psychological sequelae of cancer diagnosis: a meta-analytical review of 58 studies after 1980. *Psychosom Med*. 1997;59(3):280-293.
- Carlson LE, Bultz BD. Efficacy and medical cost offset of psychosocial interventions in cancer care: making the case for economic analyses. *Psychooncology*. 2004;13(12):837-849.
- Newport DJ, Nemeroff CB. Assessment and treatment of depression in the cancer patient. *J Psychosom Res*. 1998;45(3):215-237.

32. Walker J, Holm Hansen C, Martin P, et al. Prevalence of depression in adults with cancer: a systematic review. *Ann Oncol*. 2013;24(4):895-900.
33. Massie MJ. Prevalence of depression in patients with cancer. *J Natl Cancer Inst Monogr*. 2004;(32):57-71.
34. Dauchy S, Dolbeault S, Reich M. Depression in cancer patients. *EJC Suppl*. 2013;11(2):205-215.
35. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Distress Management. v.2.2016. <http://www.nccn.org>. Updated July 25, 2016. Accessed October 25, 2016.
36. Newell SA, Sanson-Fisher RW, Savolainen NJ. Systematic review of psychological therapies for cancer patients: overview and recommendations for future research. *J Natl Cancer Inst*. 2002;94(8):558-584.
37. Pollak KI, Arnold RM, Jeffreys AS, et al. Oncologist communication about emotion during visits with patients with advanced cancer. *J Clin Oncol*. 2007;25(36):5748-5752.
38. de Vries M, Stiefel F. Psycho-oncological interventions and psychotherapy in the oncology setting. *Recent Results Cancer Res*. 2014;197:121-135.
39. Pinquart M, Duberstein PR. Depression and cancer mortality: a meta-analysis. *Psychol Med*. 2010;40(11):1797-1810.
40. Brintzenhofe-Szoc KM, Levin TT, Li Y, Kissane DW, Zabora JR. Mixed anxiety/depression symptoms in a large cancer cohort: prevalence by cancer type. *Psychosomatics*. 2009;50(4):383-391.
41. Kissane DW, Bylund CL, Banerjee SC, et al. Communication skills training for oncology professionals. *J Clin Oncol*. 2012;30(11):1242-1247.
42. Bower JE, Bak K, Berger A, et al; American Society of Clinical Oncology. Screening, assessment, and management of fatigue in adult survivors of cancer: an American Society of Clinical Oncology clinical practice guideline adaptation. *J Clin Oncol*. 2014;32(17):1840-1850.
43. Vodermaier A, Linden W, Siu C. Screening for emotional distress in cancer patients: a systematic review of assessment instruments. *J Natl Cancer Inst*. 2009;101(21):1464-1488.
44. Grassi L, Caruso R, Sabato S, Massarenti S, Nanni MG; The UniFe Psychiatry Working Group Coauthors. Psychosocial screening and assessment in oncology and palliative care settings. *Front Psychol*. 2015;5:1485.
45. Pasacreta JV, Kenefick AL, McCorkle R. Managing distress in oncology patients: description of an innovative online educational program for nurses. *Cancer Nurs*. 2008;31(6):485-490.
46. Miovic M, Block S. Psychiatric disorders in advanced cancer. *Cancer*. 2007;110(8):1665-1676.
47. Glaesmer H, Rompell M, Brähler E, Hinz A, Maercker A. Adjustment disorder as proposed for ICD-11: dimensionality and symptom differentiation. *Psychiatry Res*. 2015;229(3):940-948.
48. Holland JC. Use of alternative medicine—a marker for distress? *N Engl J Med*. 1999;340(22):1758-1759.
49. Carta MG, Balestrieri M, Murru A, Hardoy MC. Adjustment disorder: epidemiology, diagnosis and treatment. *Clin Pract Epidemiol Ment Health*. 2009;5:15.
50. Connolly MB, Crits-Christoph P, Shappell S, Barber JP, Luborsky L. Therapist interventions in early sessions of brief supportive-expressive psychotherapy for depression. *J Psychother Pract Res*. 1998;7(4):290-300.
51. Luborsky L, Crits-Christoph P. *Understanding Transference*. New York, NY: Basic Books; 1990:15-36.
52. Crits-Christoph P, Connolly MB. Alliance and technique in short-term dynamic therapy. *Clin Psychol Rev*. 1999;19(6):687-704.
53. Spiegel D, Bloom JR, Yalom I. Group support for patients with metastatic cancer. A randomized outcome study. *Arch Gen Psychiatry*. 1981;38(5):527-533.
54. Goodwin PJ, Leszcz M, Ennis M, et al. The effect of group psychosocial support on survival in metastatic breast cancer. *N Engl J Med*. 2001;345(24):1719-1726.
55. Classen C, Butler LD, Koopman C, et al. Supportive-expressive group therapy and distress in patients with metastatic breast cancer: a randomized clinical intervention trial. *Arch Gen Psychiatry*. 2001;58(5):494-501.
56. Manber R, Bernert RA, Suh S, Nowakowski S, Siebern AT, Ong JC. CBT for insomnia in patients with high and low depressive symptom severity: adherence and clinical outcomes. *J Clin Sleep Med*. 2011;7(6):645-652.
57. Muriel AC, Hwang VS, Kornblith A, et al. Management of psychosocial distress by oncologists. *Psychiatr Serv*. 2009;60(8):1132-1134.
58. McFarland DC, Johnson Shen M, Harris K, et al. ReCAP: would women with breast cancer prefer to receive an antidepressant for anxiety or depression from their oncologist? *J Oncol Pract*. 2016;12(2):172-174, e197-e206.
59. McFarland D, Lahijani S, Holland J. Managing depression in patients with cancer. *Oncology (Williston Park)*. 2016;30(7):665-671.
60. Shultz E, Malone DA Jr. A practical approach to prescribing antidepressants. *Cleve Clin J Med*. 2013;80(10):625-631.
61. Buckland G, Travier N, Cottet V, et al. Adherence to the Mediterranean diet and risk of breast cancer in the European prospective investigation into cancer and nutrition cohort study. *Int J Cancer*. 2013;132(12):2918-2927.
62. Levenson JL, ed. *Textbook of Psychosomatic Medicine: Psychiatric Care of the Medically Ill*. 2nd ed. Washington, DC: American Psychiatric Publishing; 2011.
63. Cordova MJ, Giese-Davis J, Golant M, et al. Mood disturbance in community cancer support groups. The role of emotional suppression and fighting spirit. *J Psychosom Res*. 2003;55(5):461-467.
64. Golant MTK, Buzaglo J. The engaged patient: the cancer support community's integrative model of evidence-based psychosocial programs, services, and research. In: Holland JC, Breitbart WS, Jacobsen PB, et al, eds. *Psycho-Oncology*. 3rd ed. Oxford University Press; 2015.
65. Stern TA, Fricchione GL, Cassem NH, Jellinek M, Rosenbaum JF. *Massachusetts General Hospital: Handbook of General Hospital Psychiatry*. 6th ed. Philadelphia, PA: Mosby; 2010.
66. Fisch MJ, Zhao F, Manola J, Miller AH, Pirl WF, Wagner LI. Patterns and predictors of antidepressant use in ambulatory cancer patients with common solid tumors. *Psychooncology*. 2015;24(5):523-532.
67. Mojtabai R, Olfson M. Proportion of antidepressants prescribed without a psychiatric diagnosis is growing. *Health Aff (Millwood)*. 2011;30(8):1434-1442.
68. Akechi T, Ietsugu T, Sukigara M, et al. Symptom indicator of severity of depression in cancer patients: a comparison of the DSM-IV criteria with alternative diagnostic criteria. *Gen Hosp Psychiatry*. 2009;31(3):225-232.
69. Snyderman D, Wynn D. Depression in cancer patients. *Prim Care*. 2009;36(4):703-719.
70. Wakefield CE, Butow PN, Aaronson NA, Hack TF, Hulbert-Williams NJ, Jacobsen PB; International Psycho-Oncology Society Research Committee. Patient-reported depression measures in cancer: a meta-review. *Lancet Psychiatry*. 2015;2(7):635-647.
71. Mitchell AJ, Hussain N, Grainger L, Symonds P. Identification of patient-reported distress by clinical nurse specialists in routine oncology practice: a multicentre UK study. *Psychooncology*. 2011;20(10):1076-1083.
72. Watson M, Kissane DW, eds. *Handbook of Psychotherapy in Cancer Care*. Chichester, UK: John Wiley & Sons; 2011:105-117.
73. Carlson LE, Beattie TL, Giese-Davis J, et al. Mindfulness-based cancer recovery and supportive-expressive therapy maintain telomere length relative to controls in distressed breast cancer survivors. *Cancer*. 2015;121(3):476-484.
74. Montgomery GH, Schnur JB, Kravits K. Hypnosis for cancer care: over 200 years young. *CA Cancer J Clin*. 2013;63(1):31-44.
75. Breitbart W, Poppito S, Rosenfeld B, et al. Pilot randomized controlled trial of individual meaning-centered psychotherapy for patients with advanced cancer. *J Clin Oncol*. 2012;30(12):1304-1309.
76. Breitbart W, Rosenfeld B, Pessin H, Applebaum A, Kulikowski J, Lichtenhal WG. Meaning-centered group psychotherapy: an effective intervention for improving psychological well-being in patients with advanced cancer. *J Clin Oncol*. 2015;33(7):749-754.
77. Breitbart W, Alici Y. Evidence-based treatment of delirium in patients with cancer. *J Clin Oncol*. 2012;30(11):1206-1214.
78. Stagno D, Gibson C, Breitbart W. The delirium subtypes: a review of prevalence, phenomenology, pathophysiology, and treatment response. *Palliat Support Care*. 2004;2(2):171-179.
79. Breitbart W, Tremblay A, Gibson C. An open trial of olanzapine for the treatment of delirium in hospitalized cancer patients. *Psychosomatics*. 2002;43(3):175-182.
80. Brown LF, Kroenke K, Theobald DE, Wu J, Tu W. The association of depression and anxiety with health-related quality of life in cancer patients with depression and/or pain. *Psychooncology*. 2010;19(7):734-741.
81. Breitbart W. Psychiatric management of cancer pain. *Cancer*. 1989;63(11)(suppl):2336-2342.
82. Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC. The biopsychosocial approach to chronic pain: scientific advances and future directions. *Psychol Bull*. 2007;133(4):581-624.
83. O'Mahony S, Goulet J, Kornblith A, et al. Desire for hastened death, cancer pain and depression: report of a longitudinal observational study. *J Pain Symptom Manage*. 2005;29(5):446-457.