

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Distress Management

Version 2.2024 — March 22, 2024

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National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2024 Distress Management

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NCCN Distress Management Panel Members Summary of the Guidelines Updates

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Key Terms:

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- Distress and Definition of Distress in Cancer (DIS-1)
- Standards of Care for Distress Management (DIS-2)

Overview of Evaluation and Treatment Process (DIS-3) Management of Expected Distress Symptoms (DIS-4)

NCCN Distress Thermometer and Problem List (DIS-A) Psychosocial Distress Patient Characteristics (DIS-B)

Psychological/Psychiatric Treatment Guidelines (DIS-5) Social Work and Counseling Services: Practical Problems (DIS-22) Social Work and Counseling Services: Psychosocial Problems (DIS-23) Chaplaincy Care (DIS-24) Principles for Implementation of Standards and Distress Management Guidelines (DIS-25) Institutional Evaluation of Standards of Care (DIS-26)

Clinical Trials: NCCN believes that the best management for any patient with cancer is in a clinical trial.

Participation in clinical trials is especially encouraged.

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NCCN Categories of Evidence and Consensus: All recommendations are category 2A unless otherwise indicated.

See NCCN Categories of Evidence and Consensus.

Abbreviations (ABBR-1)

For Non-Pain Symptom Management and Palliative Issues, see the NCCN Guidelines for Palliative Care For Cancer Pain, see the NCCN Guidelines for Adult Cancer Pain

The NCCN Guidelines[®] are a statement of evidence and consensus of the authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult the NCCN Guidelines is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network® (NCCN®) makes no representations or warranties of any kind regarding their content, use or application and disclaims any responsibility for their application or use in any way. The NCCN Guidelines are copyrighted by National Comprehensive Cancer Network[®]. All rights reserved. The NCCN Guidelines and the illustrations herein may not be reproduced in any form without the express written permission of NCCN. ©2024.

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Terminologies in all NCCN Guidelines are being actively modified to advance the goals of equity, inclusion, and representation.

Updates in Version 2.2024 of the NCCN Guidelines for Distress Management from Version 1.2024 include:

MS-1

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The discussion section has been updated to reflect the changes in the algorithm.

Updates in Version 1.2024 of the NCCN Guidelines for Distress Management from Version 2.2023 include:

Global Changes

• Referral to psychiatry recommendations updated throughout the guideline.

DIS-2

• Bullet added: Because experiences of prejudice and discrimination may contribute significantly to distress, particularly among individuals with mental illness and other groups that have been marginalized or made vulnerable, health care systems should ensure a culture of diversity, equity, and inclusiveness in the management of cancer-related distress.

DIS-A

· Problem List, social concerns, bullet added: Prejudice or discrimination

DIS-B

- Patients at increased risk for distress
- > 7th bullet, 12th sub-bullet modified: Discrimination or prejudice

DIS-6

• Evaluation, impairment present

Thought disorder/psychosis pathway modified: Arrange for ongoing primary psychiatric management Evaluate for safety and consider referral to psychiatrv.

DIS-8

Option modified: pharmacotherapy psychiatric medication (Also for DIS-20).

DIS-9

- Treatment, bullet modified: "Consider referral to social work, and counseling, services or chaplaincy care..." (Also for DIS-11, DIS-16, DIS-17). **DIS-10**
- Treatment, no/partial response, bullet 4 modified: Re-evaluate psychotherapeutic intervention and consider higher level care with intensive outpatientprogram diagnosis and treatment (Also for DIS-12).

DIS-13

• Evaluation, option modified: No active signs symptoms of psychosis.

DIS-14

Consider transfer admission to psychiatric unit/hospital

DIS-15

Reevaluate medication (consider antipsychotics), psychotherapy, support, education

DIS-20

• Motivated to guit/cut back, bullet 1 modified: Referral to addiction medicine or outpatient substance use program.

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"DISTRESS"

The term "distress" was chosen because it:

- Is more acceptable and less stigmatizing than "psychiatric," "psychosocial," or "emotional"
- Sounds "normal" and less embarrassing
- Can be defined and measured by self-report

DEFINITION OF DISTRESS IN CANCER

Distress is a multifactorial unpleasant experience of a psychological (ie, cognitive, behavioral, emotional), social, spiritual, and/or physical nature that may interfere with one's 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.

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STANDARDS OF CARE FOR DISTRESS MANAGEMENT

- Distress should be recognized, monitored, documented, and treated promptly at all stages of disease and in all settings.
- Screening should identify the level and nature of the distress.

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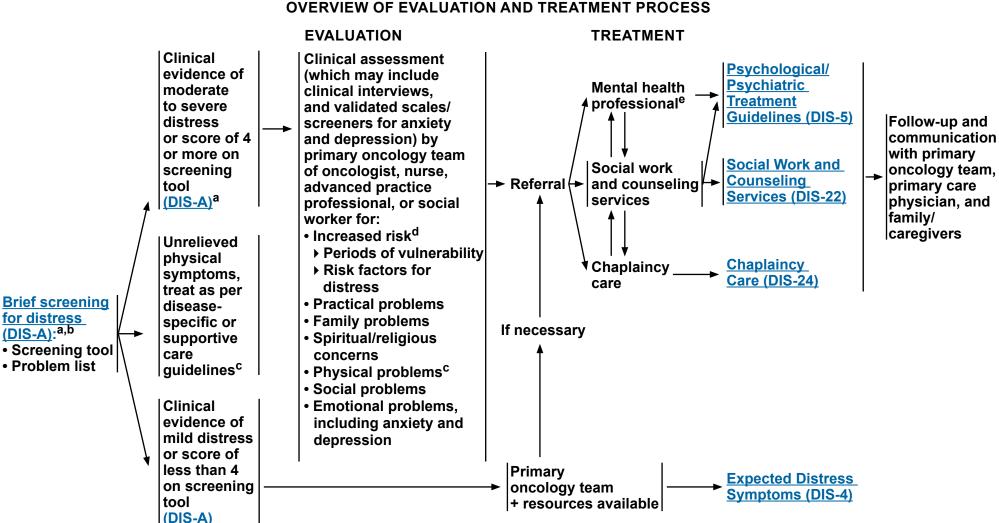
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- Ideally, patients should be screened for distress at every medical visit as a hallmark of patient-centered care. At a minimum, patients should be screened for distress at their initial visit, at appropriate intervals, and as clinically indicated, especially with changes in disease status (ie, remission, recurrence, progression, treatment-related complications).
- Distress should be assessed and managed according to clinical practice guidelines.
- Interdisciplinary institutional committees should be formed to implement standards for distress management.
- Educational and training programs should be developed to ensure that health care professionals and certified chaplains have knowledge and skills in the assessment and management of distress.
- Licensed mental health professionals and certified chaplains experienced in psychosocial aspects of cancer should be readily available as staff members or by referral.
- Medical care contracts should include adequate reimbursement for services provided by mental health professionals.
- Clinical health outcomes measurement should include assessment of the psychosocial domain (eg, quality of life and patient and family satisfaction).
- Patients, families, and treatment teams should be informed that distress management is an integral part of total medical care and is provided with appropriate information about psychosocial services in the treatment center and the community.
- Quality of distress management programs/services should be included in institutional continuous quality improvement (CQI) projects.
- Because experiences of prejudice and discrimination may contribute significantly to distress, particularly among individuals with mental illness and other groups that have been marginalized or made vulnerable, health care systems should ensure a culture of diversity, equity, and inclusiveness in the management of cancer-related distress.



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^a The NCCN Problem List and the NCCN Distress Thermometer Screening Tool may be modified to fit the needs of the local population.

^b See Discussion (MS-8) for information about other validated screening tools.

^c Consider referral for palliative care management (see NCCN Guidelines for Palliative Care and NCCN Guidelines for Adult Cancer Pain).

^d Psychosocial Distress Patient Characteristics (DIS-B).

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^e Psychiatrist, psychologist, advanced practice clinicians, or social worker.

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

Refer to NCCN **Guidelines** Table of Contents for Supportive Care Guidelines

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MANAGEMENT OF EXPECTED DISTRESS SYMPTOMS			
EXPECTED DISTRESS SYMPTOMS ^d	INTERVENTIONS	RE-EVALUATION	
 Fear and worry about the future Concerns about illness Sadness about loss of usual health Anger, feeling out of control Poor sleep (NCCN Guidelines for Survivorship; Sleep Disorders [SSD-1]) Poor appetite Poor concentration Preoccupation with thoughts of illness and death Concerns with treatment side effects Concerns about social role (eg, as parent) Spiritual/existential concerns Financial worries 	 Acknowledge/validate distress Clarify diagnosis, treatment options, and side effects Be sure patient understands disease and treatment options Discuss advance care planning Refer to appropriate patient education materials (eg, NCCN Guidelines for Patients) Educate patient that points of transition may bring increased vulnerability to distress Ensure continuity of care Mobilize resources Consider medication to manage symptoms: Analgesics (NCCN Guidelines for Adult Cancer Pain) Anxiolytics Hypnotics Antidepressants Psychostimulants Support groups and/or individual counseling including evidence-based interventions Family/couple/caregiver support and counseling Relaxation, mindfulness, meditation, creative therapies (eg, art, dance, music) Spiritual support Exercise Assess and strengthen coping strategies 	Monitor functional level and reevaluate as appropriate Increased or persistent distress Score ≥4 or moderate to severe distress (DIS-3)	

Note: All recommendations are category 2A unless otherwise indicated.

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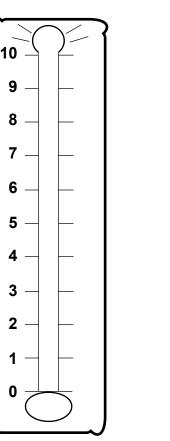
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NCCN DISTRESS THERMOMETER

Distress is an unpleasant experience of a mental, physical, social, or spiritual nature. It can affect the way you think, feel, or act. Distress may make it harder to cope with having cancer, its symptoms, or its treatment.

Instructions: Please circle the number (0–10) that best describes how much distress you have been experiencing in the past week, including today.

Extreme distress



No distress

PROBLEM LIST

Have you had concerns about any of the items below in the past week, including today? (Mark all that apply)

Physical Concerns

- Pain
- Sleep
- Fatigue
- Tobacco use
- Substance use
- □ Memory or concentration
- Sexual health
- □ Changes in eating
- Loss or change of physical abilities

Emotional Concerns

- Worry or anxiety
- Sadness or depression
- Loss of interest or enjoyment
- Grief or loss

Fear

- Loneliness
- Anger
- □ Changes in appearance
- Feelings of worthlessness or being a burden

Social Concerns

- □ Relationship with spouse or partner
- Relationship with children
- □ Relationship with family members
- Relationship with friends or coworkers
- Communication with health care team
- □ Ability to have children
- Prejudice or discrimination

Practical Concerns

- □ Taking care of myself
- □ Taking care of others
- Work
- School
- Housing
- □ Finances
- Insurance
- □ Transportation
- Child care
- Having enough food
- Access to medicine
- Treatment decisions

Spiritual or Religious Concerns

- □ Sense of meaning or purpose
- Changes in faith or beliefs
- Death, dying, or afterlife
- Conflict between beliefs and cancer treatments
- Relationship with the sacred
- Ritual or dietary needs

Other Concerns:

Note: All recommendations are category 2A unless otherwise indicated.

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PSYCHOSOCIAL DISTRESS PATIENT CHARACTERISTICS¹

PATIENTS AT INCREASED RISK FOR DISTRESS

- History of psychiatric disorder or substance use disorder
- History of depression/suicide attempt
- History of trauma and/or abuse
- (ie, physical, sexual, emotional, verbal)
- Cognitive impairment
- Communication barriers²
- Severe comorbid illnesses
- Social issues:

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- **◊** Family/caregiver conflicts
- ♦ Inadequate social support
- ♦ Social isolation
- ◊ Living alone
- ♦ Financial problems
- ◊ Limited access to medical care
- ♦ Young or dependent children
- ♦ Adolescent and younger adults³
- ♦ Sexual health concerns
- ♦ Fertility concerns³
- ♦ Immigration status
- ♦ Discrimination or prejudice
- ◊ Loss of stable housing/shelter/living environment
- ♦ Current substance use
- ♦ Other stressors
- Spiritual/religious concerns
- Uncontrolled symptoms
- Cancer type associated with risk of depression (eg, pancreatic cancer, head and neck cancer)

PERIODS OF INCREASED VULNERABILITY

- Diagnosis
 - ♦ Finding and investigating a suspicious symptom
 - ♦ Undergoing diagnostic workup
 - ♦ Finding out the diagnosis
 - **Or Receiving and living with an advanced cancer** diagnosis
 - ◊ Learning about genetic/familial cancer risk
- Treatment
 - Awaiting treatment
 - **Or Experiencing an increase in symptom burden**
 - **O Experiencing significant treatment-related** complication(s)
 - **Output** Experiencing an admission to/discharge from hospital
 - **Output** Experiencing changes in treatment modality
 - ♦ Experiencing disease that progresses during treatment
- End of active treatment

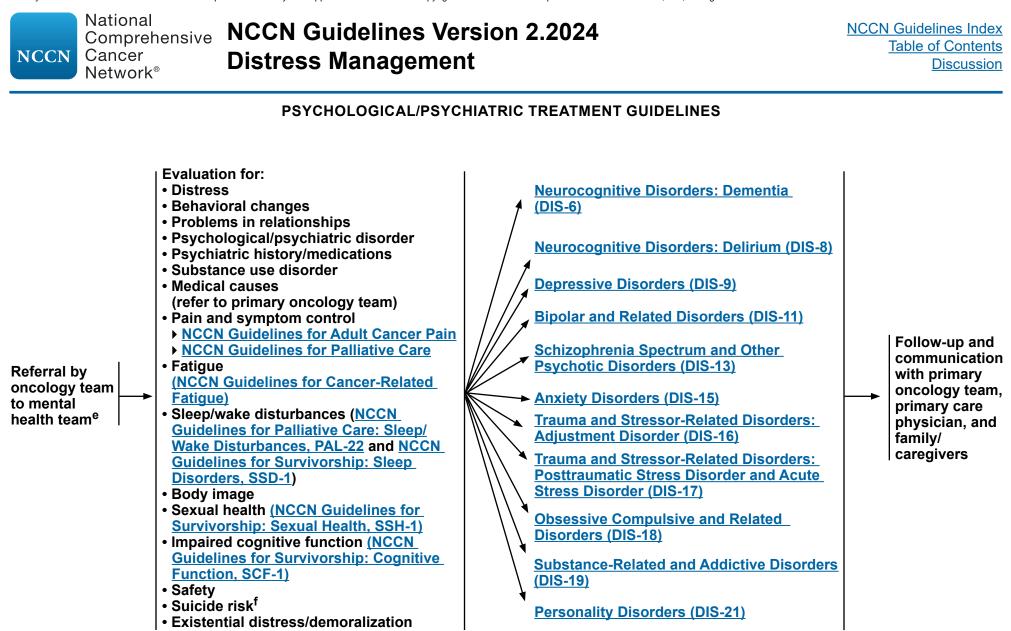
 - ♦ Transitioning to survivorship
 - ◊ Experiencing recurrence/progression of disease
 - ◊ Transitioning to end-of-life care
 - ♦ Experiencing grief and loss (eg. relative, friend, pet)

¹ For site-specific symptoms with major psychosocial consequences, see Holland JC, Golant M, Greenberg DB, et al. Psycho-oncology: A quick reference on the psychosocial dimensions of cancer symptom management. Oxford University Press, 2015.

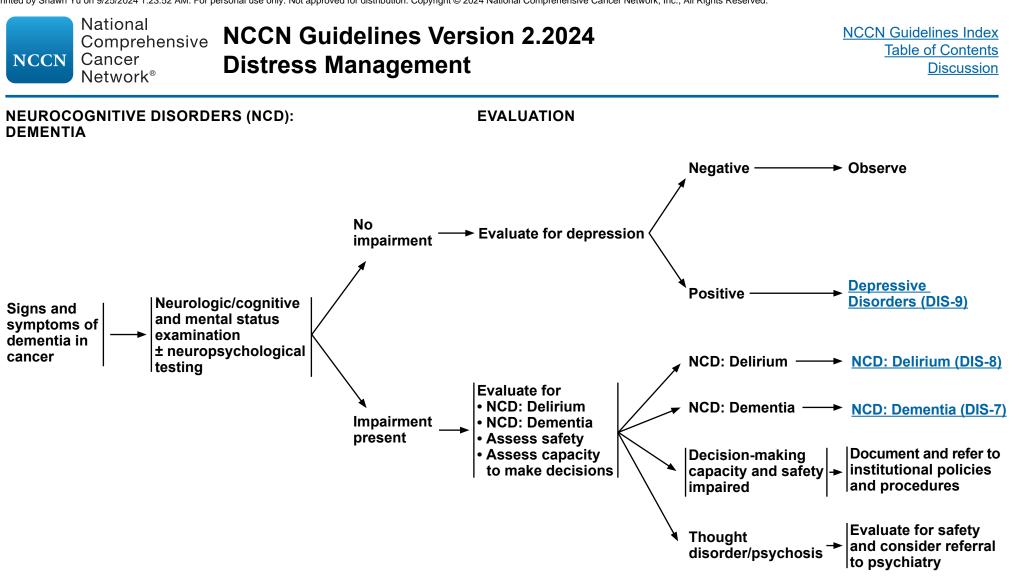
² Communication barriers include language, literacy, and physical barriers.

³ NCCN Guidelines for Adolescent and Young Adult (AYA) Oncology.

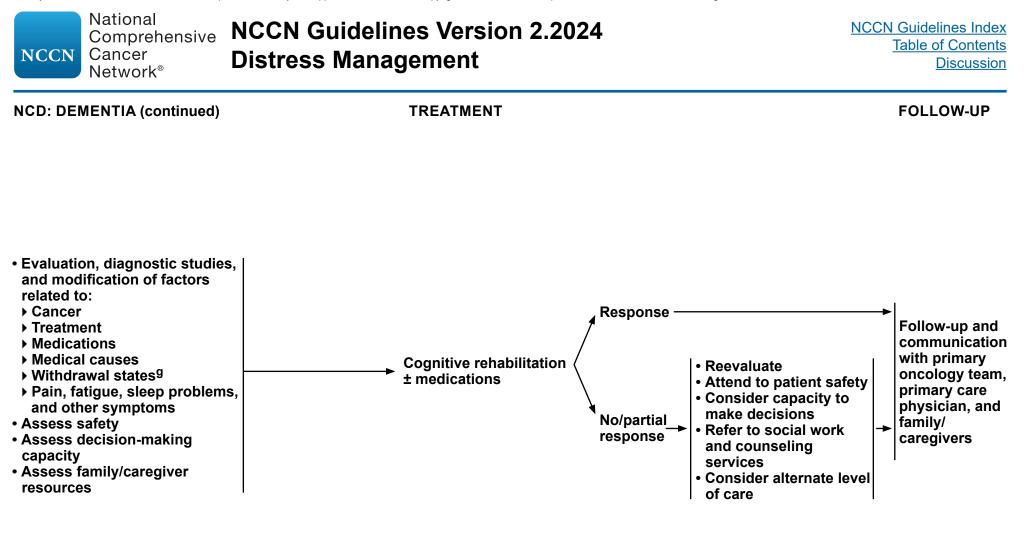
Note: All recommendations are category 2A unless otherwise indicated.



^e Psychiatrist, psychologist, advanced practice clinicians, and/or social worker. ^f Formal assessment should be conducted as per <u>The Joint Commission's Suicide Prevention Recommendations</u>.



Return to Psychological/Psychiatric Treatment Guidelines (DIS-5)

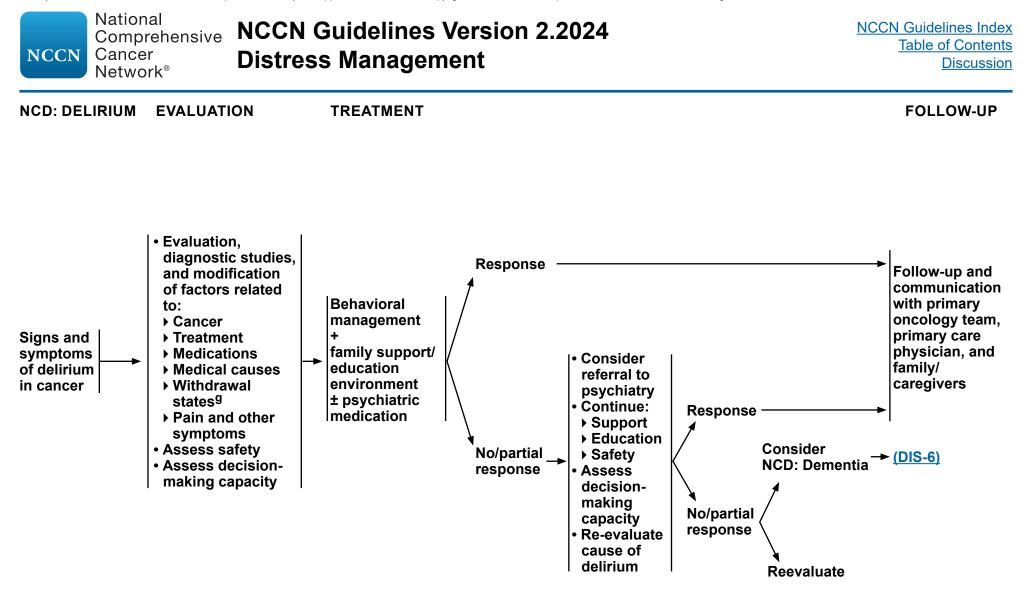


^g Management of withdrawal states may vary depending upon the substance.

Return to Psychological/Psychiatric Treatment Guidelines (DIS-5)

Note: All recommendations are category 2A unless otherwise indicated. Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

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^g Management of withdrawal states may vary depending upon the substance.

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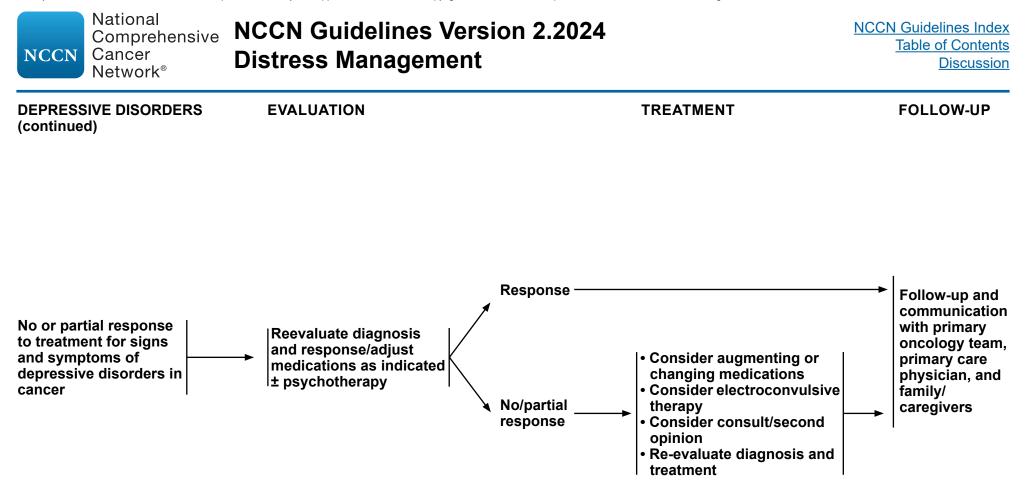


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DEPRESSIVE DISORDERS	EVALUATION		TREATMENT		FOLLOW-UP
Signs and symptoms of the following disorders: • Depressive disorders related to medical illness • Major depressive disorders • Persistent depressive disorder	 Evaluation, diagnostic studies, and modification of factors related to: Cancer Treatment Medications Medical causes Withdrawal states Pain Fatigue Sleep disruption Anorexia Anhedonia Decreased interest in activities Wish to die 	No danger to self or —► others	 Psychotherapy Optimal management of physical symptoms contributing to depression Psychotropic medication (category 1) Mental health treatment and follow-up/patient and family education Consider referral to psychiatry Consider referral to social work, counseling, or chaplaincy care. See <u>Social Work and</u> <u>Counseling Services (DIS-22)</u> or <u>Chaplaincy Care (DIS-24)</u> 	Response — No/partial — response	Follow-up and communication with primary oncology team, primary care physician, and family/ caregivers
	 Suicidal thoughts Mood swings Poor concentration Demoralization Anxiety Consider psychosocial and spiritual concerns Assess decision-making capacity Assess safety Evaluate family/home environment Evaluate alcohol and recreational drug use Evaluate using validated tool (eg, PHQ-2 or PHQ-9) 	Danger to self or others	 Further evaluate suicide and homicide risk Consider directing patient to the emergency department for further psychiatric evaluation Assure patient safety: Consider referral to psychiatry Increase monitoring Safety planning Remove any guns and other dangerous objects Assure safety of others Consider referral to social work, counseling, or chaplaincy care. See Social Work and Counseling Services (DIS-22) or Chaplaincy Care (DIS-24) 	Psychi	Follow-up and communication with primary oncology team, primary care physician, and family/ caregivers

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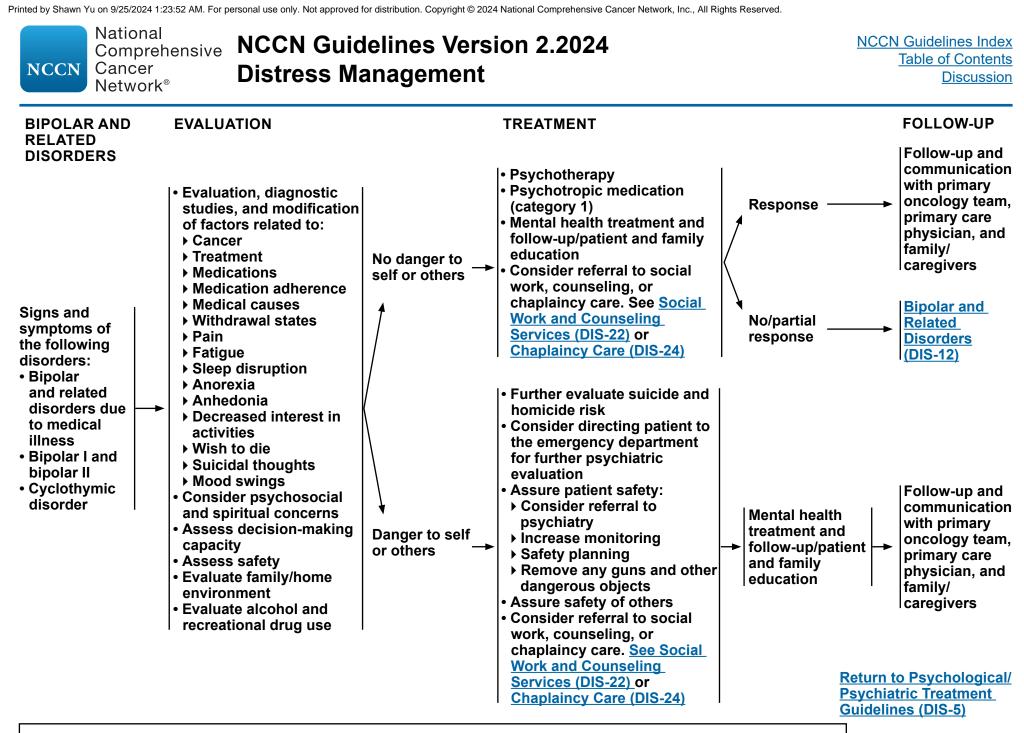
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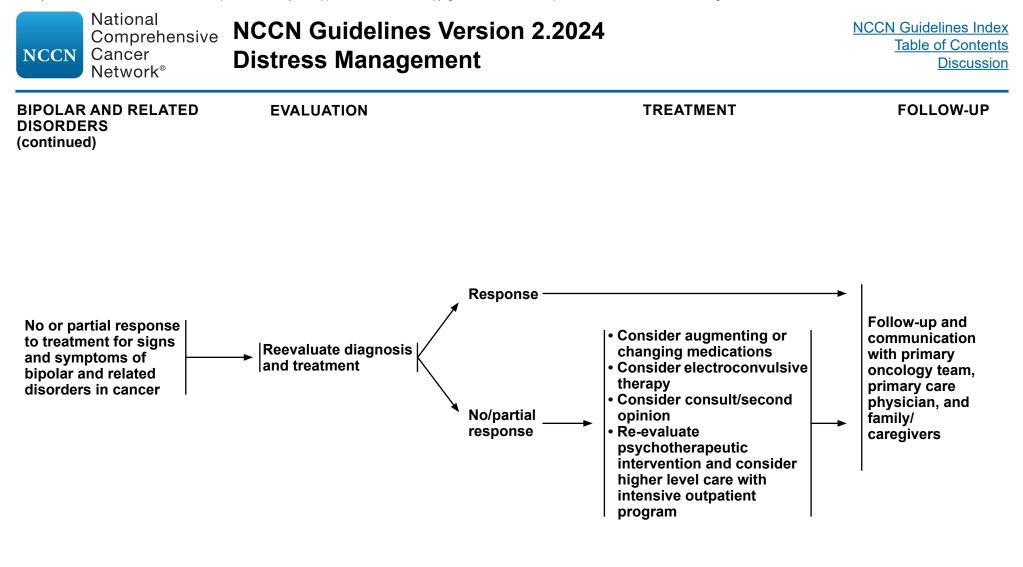
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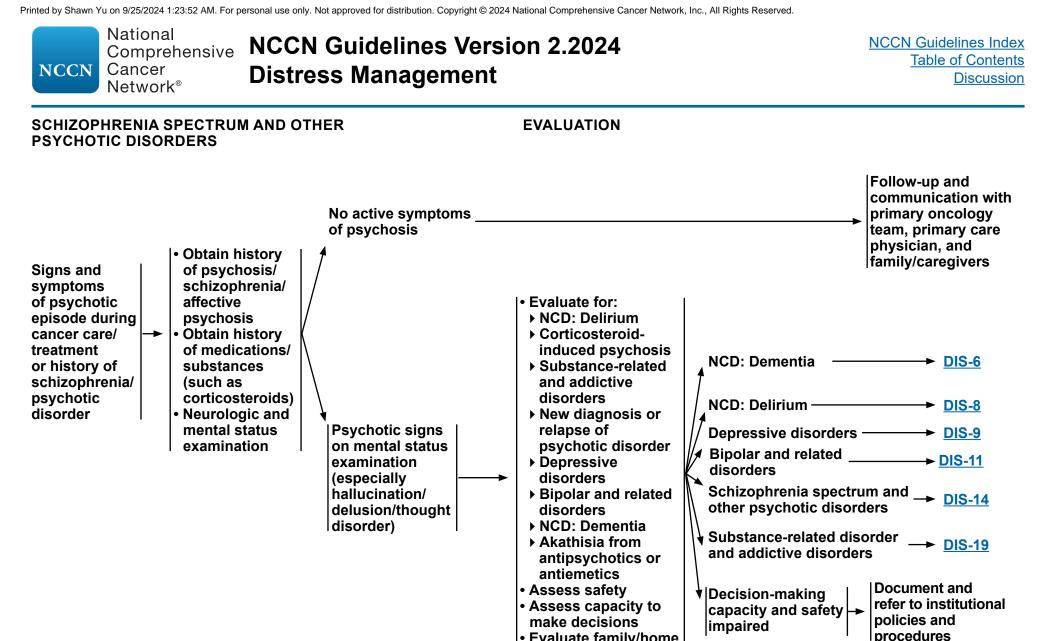
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Return to Psychological/Psychiatric Treatment Guidelines (DIS-5)

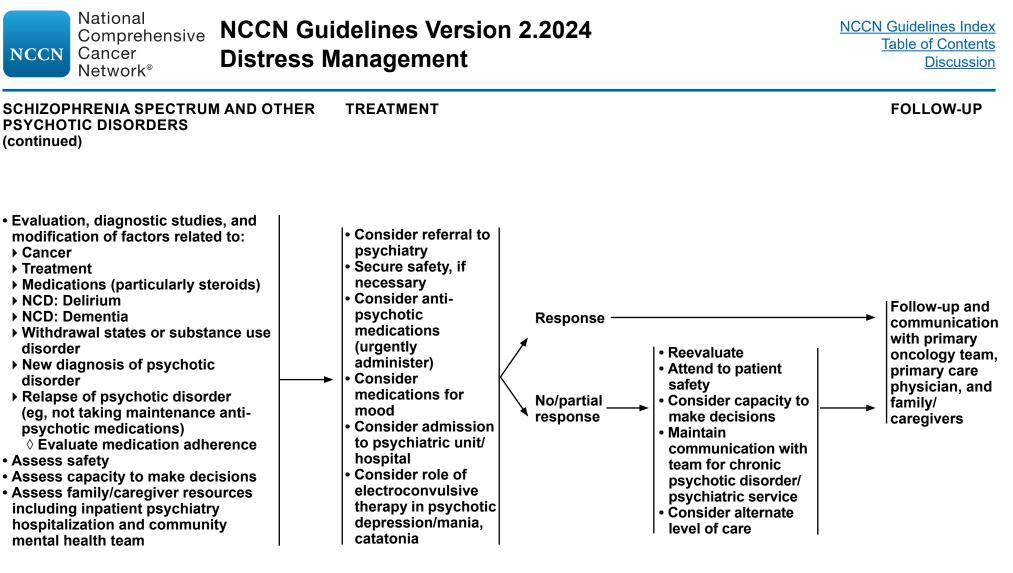


Evaluate family/home environment

Return to Psychological/Psychiatric Treatment Guidelines (DIS-5)

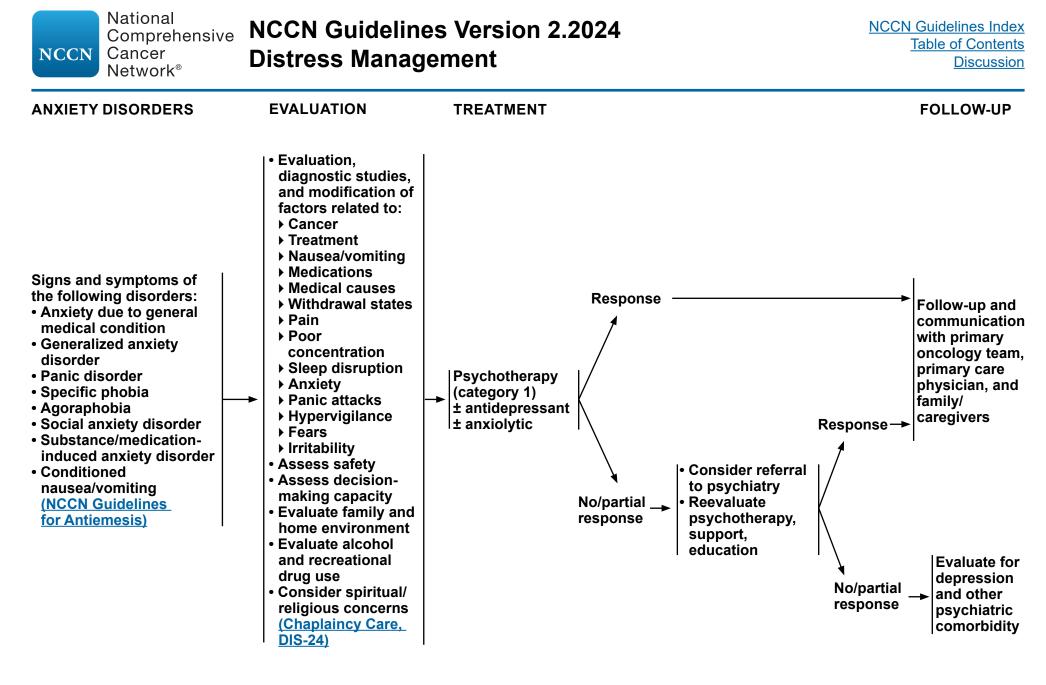
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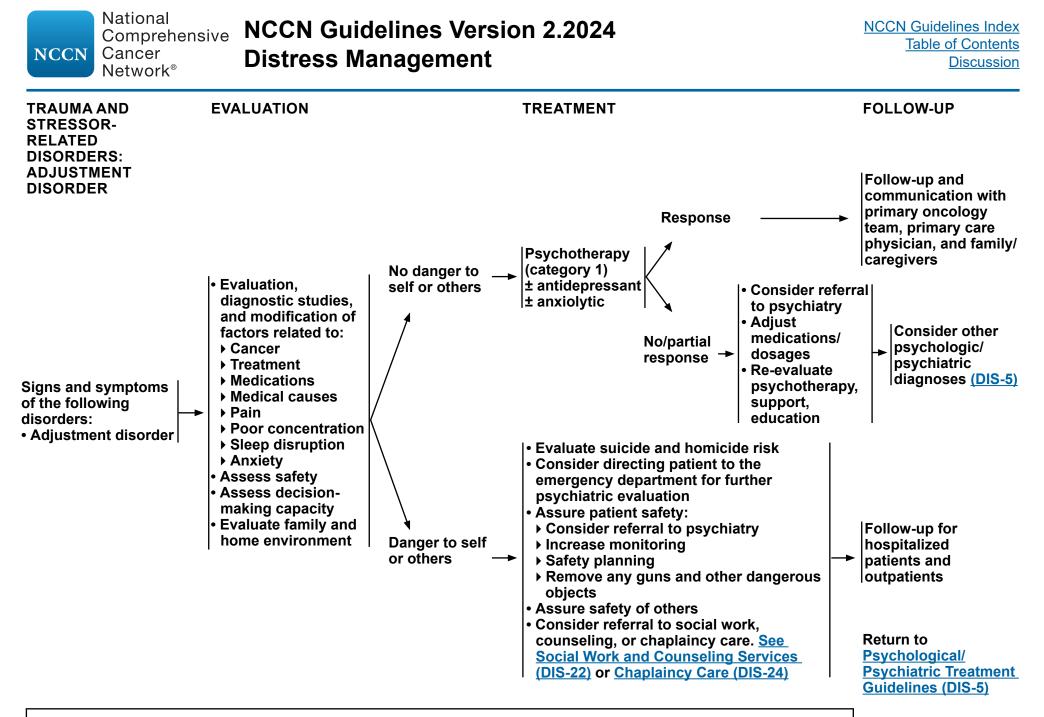


Return to Psychological/Psychiatric Treatment Guidelines (DIS-5)

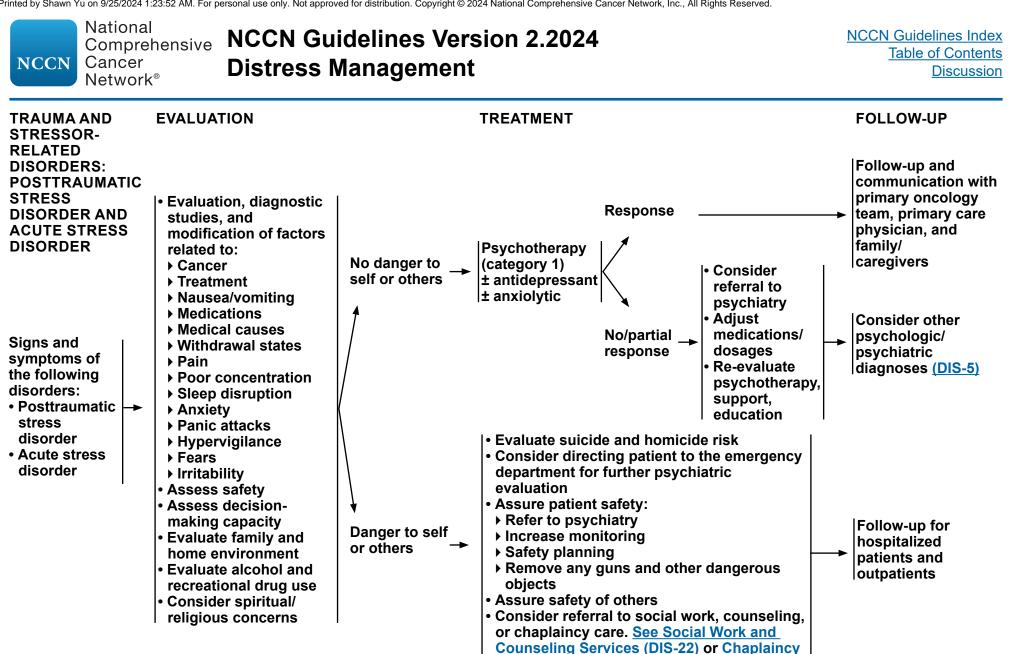
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Return to Psychological/Psychiatric Treatment Guidelines (DIS-5)



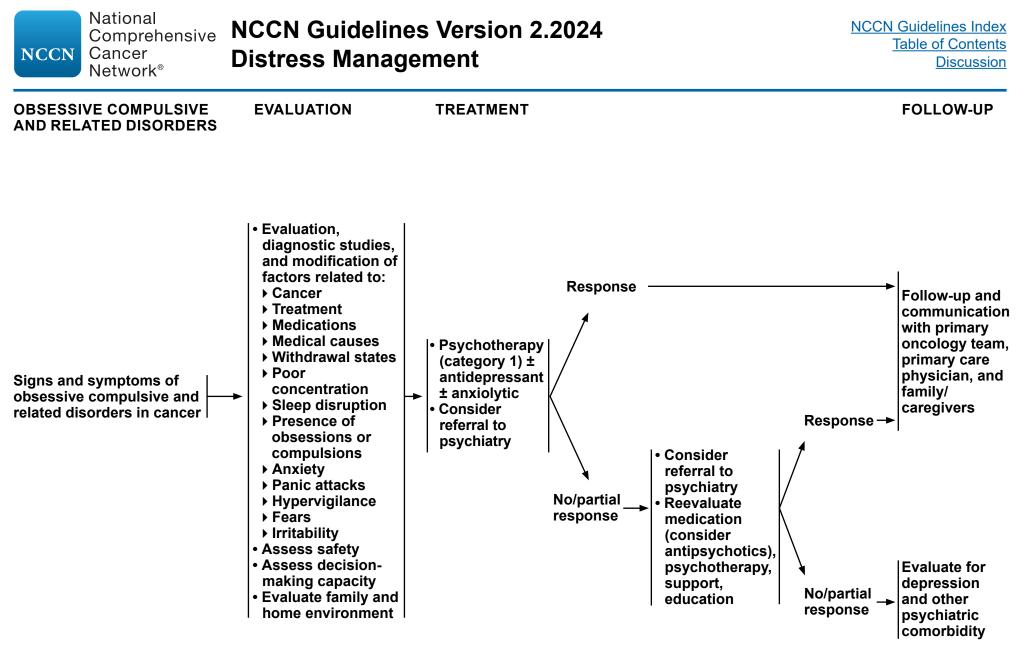
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Care (DIS-24)

Return to Psychological/Psychiatric Treatment Guidelines (DIS-5)

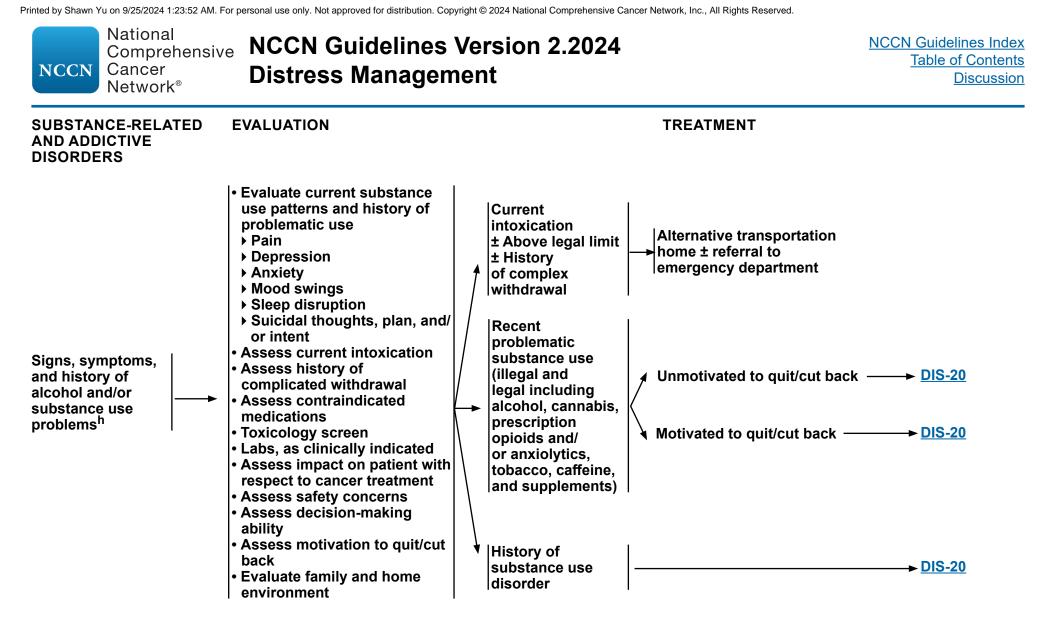
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Return to Psychological/Psychiatric Treatment Guidelines (DIS-5)

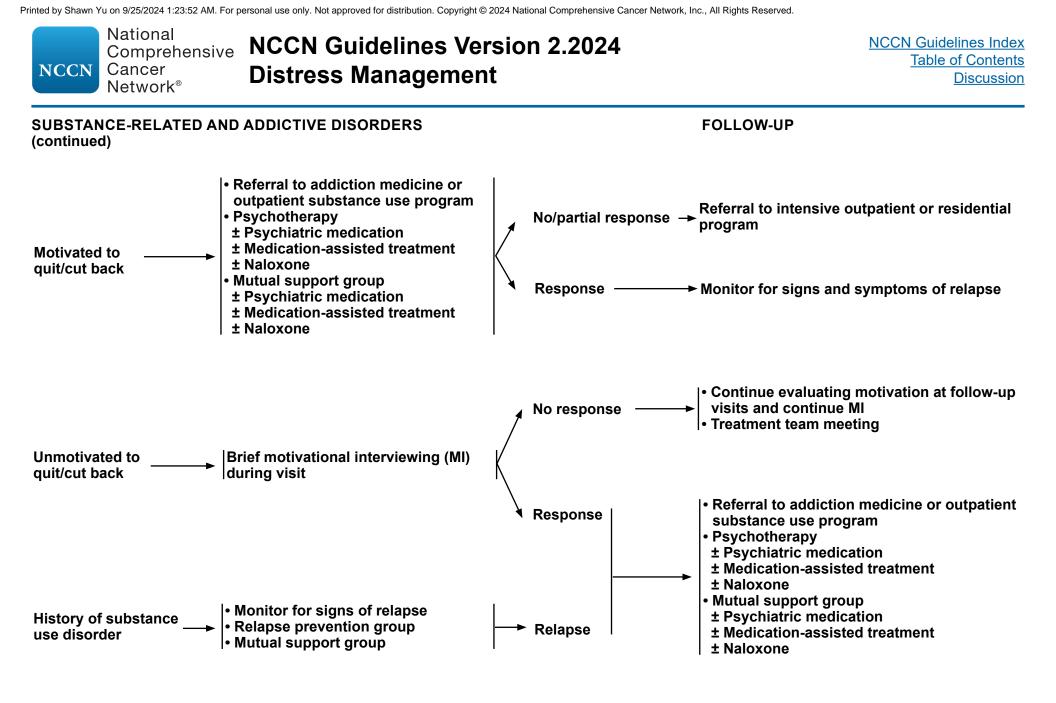
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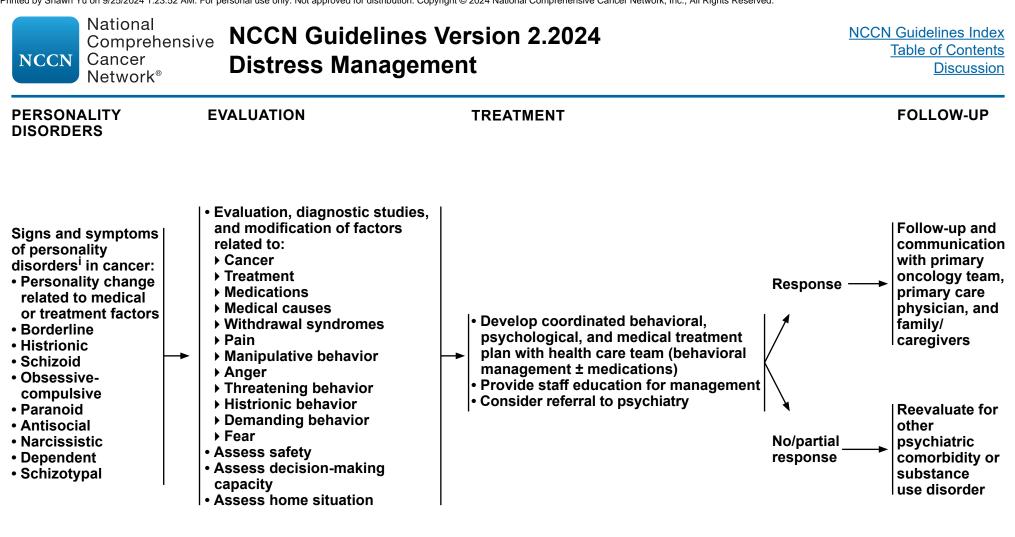


^h Opioids, alcohol, tobacco, or other. For opioids, also see Opioid Principles, Prescribing, Titration, Maintenance, and Safety in the <u>NCCN Guidelines for Adult Cancer Pain (PAIN-E)</u>. For tobacco use see the <u>NCCN Guidelines for Smoking Cessation</u>. Return to Psychological/ Psychiatric Treatment Guidelines (DIS-5)

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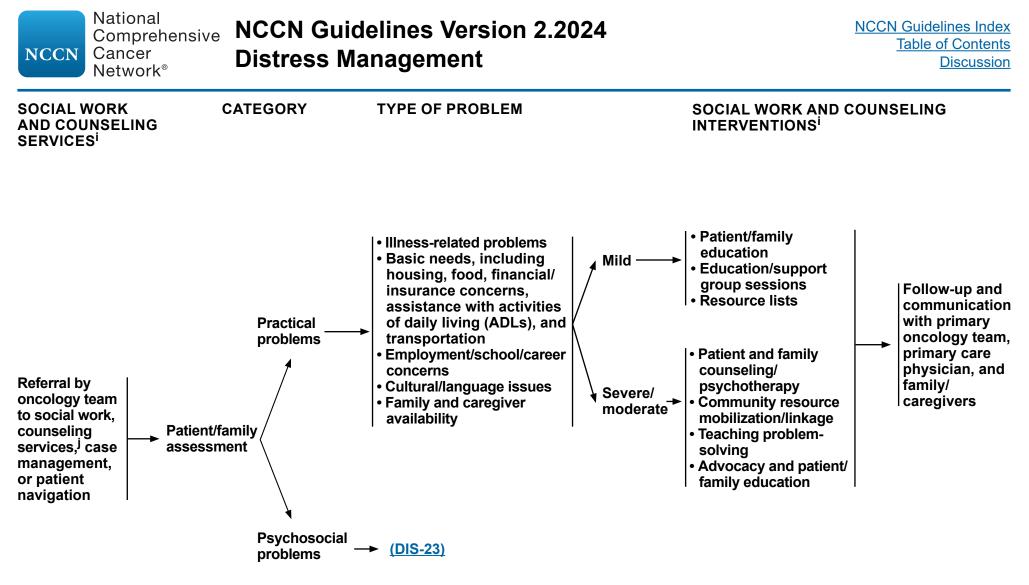


Return to Psychological/Psychiatric Treatment Guidelines (DIS-5)

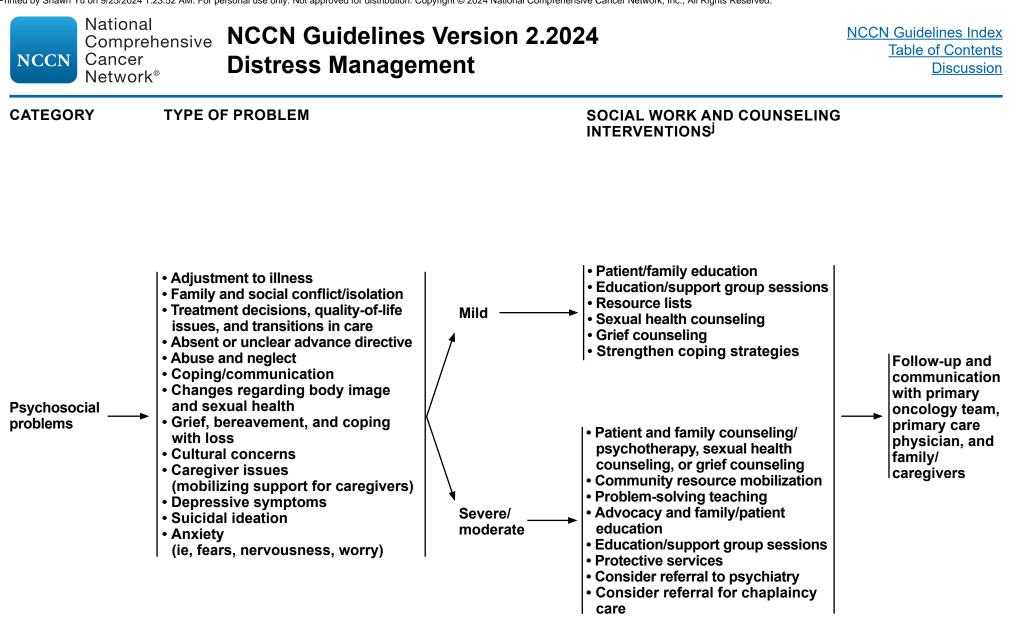


ⁱ For a complete list of personality disorders, see the American Psychiatric Association (2013). Diagnostic and Statistical Manual of	Return to Psychological/ Psychiatric Treatment
Mental Disorders (5th ed., Text Revision). Arlington, VA: American Psychiatric Press, Inc.	Guidelines (DIS-5)

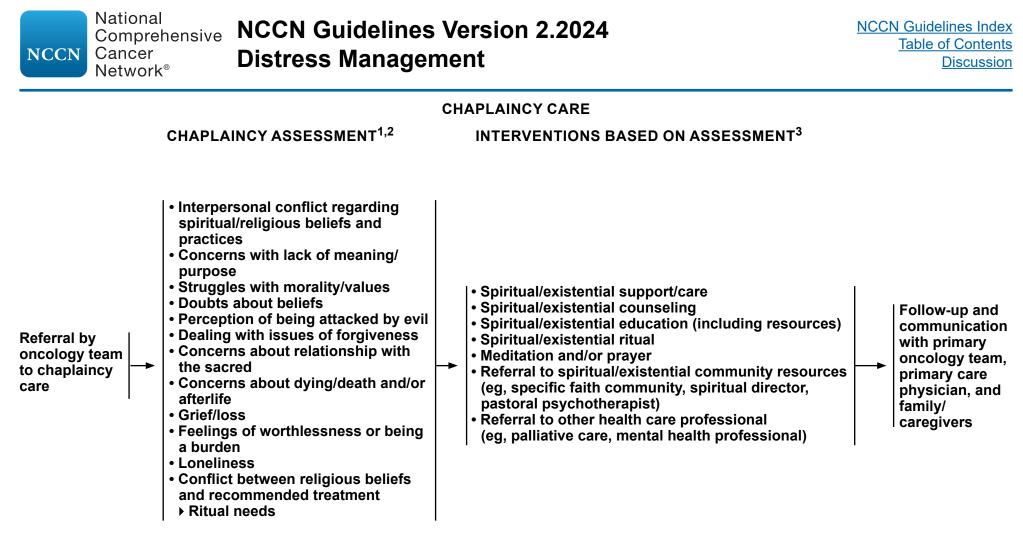
Note: All recommendations are category 2A unless otherwise indicated.



^j Social work and counseling services include mental health care as described in the psychological/psychiatric treatment guidelines (DIS-5).



^j Social work and counseling services include mental health care as described in the psychological/psychiatric treatment guidelines (DIS-5).



¹ Exline JJ, Pargament KI, Grubbs JB, Yali AM. The Religious and Spiritual Struggles Scale: Development and initial validation. Psychology of Religion and Spirituality 2014;6:208-222.

² van Bruggen V, Ten Klooster P, Westerhof G, et al. The Existential Concerns Questionnaire (ECQ)-development and initial validation of a new existential anxiety scale in a nonclinical and clinical sample. J Clin Psychol 2017;73:1692-1703.

³ Spiritual Health Victoria spiritual care standards: <u>https://spiritualhealth.org.au/standards</u>.

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PRINCIPLES FOR IMPLEMENTATION OF STANDARDS AND DISTRESS MANAGEMENT GUIDELINES⁴⁻¹¹

The Commission on Cancer's accreditation standards include screening all patients with cancer for psychosocial distress and referral for psychosocial care as needed.¹²

- Recommend creation of a work group/cancer committee, which should be composed of multiple disciplines' representatives, including but not limited to physician champions, nurses, psychologists, information technology experts, administrative leadership, social workers, and chaplaincy.
- Explicit support and backing of the institutional leadership is essential. The committee should identify and organize advocates and institutional stakeholders who will support the implementation of the program. A small-scale pilot program may be a preferable way to test the screening process before a larger scale implementation is put in place.
- The following should be considered:

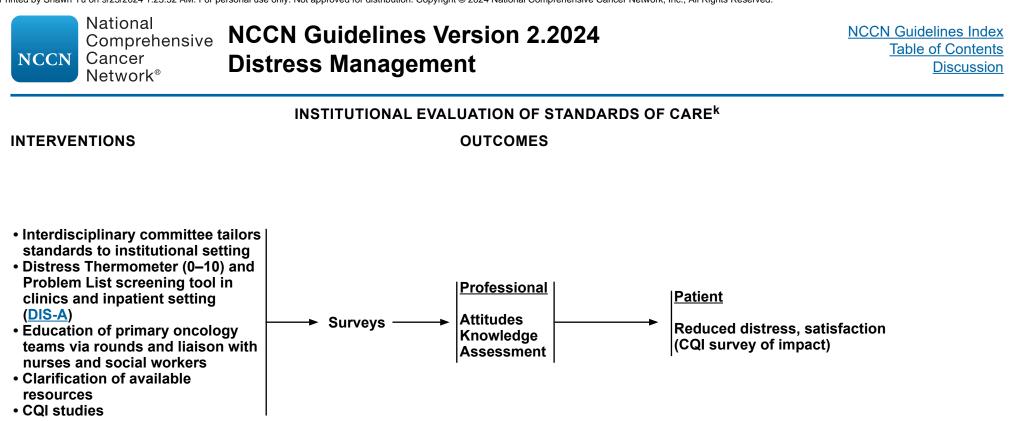
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- Already existing resources (eq, screening tools or programs already in place)
- > Current workflows, processes, and available technologies
- Various distress screening tools have been developed, including the NCCN Distress Thermometer and Problem List (DIS-A). The cancer committee should select the most appropriate screening tool to be administered in its setting.
- Standardized, validated instruments, or tools with established clinical cutoffs, are recommended.
- Determine the cutoff score or specific problems that will be used to identify distressed patients.
- Determine the frequency of screening.
- Develop a response algorithm (ie, who is alerted to screening results, how information is processed, and triggering of appropriate referrals).
- > Develop a process in which distress screening results are made known to critical members of the care team, including such strategies as incorporating the results into the patient's medical record.
- > Develop results thresholds for generating respective referrals. These may vary based on types of services available and their capacity.
- Consider incorporating distress screening into the institutions' quality improvement and assessment process (eq. distress screening becomes a measurable quality metric).
- > Distress screening and response to results data should be tracked and can be used for further improvements, as well as expansion of needed services.

⁴ Ehlers SL, Davis K, Bluethmann SM, et al. Screening for psychosocial distress	⁸ Knies AK, Jutagir DR, Ercolano E, et al. Barriers and facilitators to implementing the commission on cancer's distress screening program standard. Palliat Support Care 2019;17:253-261.
among patients with cancer: implications for clinical practice, healthcare policy, and dissemination to enhance cancer survivorship. Transl Behav Med 2019;9:282-291.	⁹ Fitch MI, Ashbury F, Nicoll I. Reflections on the implementation of screening for distress (sixth vital sign) in Canada: key lessons learned. Support Care Cancer 2018;26:4011-4020.
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Note: All recommendations are category 2A unless otherwise indicated.



^k Based on implementation/evaluation of pain management guidelines.

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ABBREVIATIONS

ADLs activities of daily living

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- CQI continuous quality improvement
- MI motivational interviewing
- NCD neurocognitive disorders

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NCCN Categories of Evidence and Consensus		
Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.	
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.	
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.	
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.	

All recommendations are category 2A unless otherwise indicated.



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Discussion This discussion corresponds to the NCCN Guidelines for Distress Management. Last updated: March 22, 2024.

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Overview

In the United States, it is estimated that there are more than 18 million individuals with a history of cancer,¹ with a total of 2,001,140 new cancer cases estimated to occur in 2024.² All patients experience some level of distress associated with their cancer diagnosis and the effects of the disease and its treatment regardless of the stage of disease. Distress can result from the reaction to the cancer diagnosis and to the various transitions throughout the trajectory of the disease, including during survivorship. Clinically significant levels of distress occur in a subset of patients, and identification and treatment of distress are of utmost importance.

These NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Distress Management discuss the identification and treatment of psychosocial problems in patients with cancer. They are intended to assist oncology teams to identify patients who require referral to psychosocial resources and to give oncology teams guidance on interventions for patients with mild distress. These Guidelines also provide guidance for social workers, certified chaplains, and mental health professionals by describing treatments and interventions for various psychosocial problems as they relate to patients with cancer.

Literature Search Criteria and Guidelines Update Methodology

Prior to the update of this version of the NCCN Guidelines[®] for Distress Management, an electronic search of the PubMed database was performed to obtain key literature, using the following search terms: (cancer distress) or (cancer depression) or (cancer anxiety) or (cancer dementia) or (cancer delirium) or (cancer depressive) or (cancer bipolar) (cancer post-traumatic stress) or (cancer acute stress) or (cancer adjustment disorder) or (cancer obsessive-compulsive disorder) or (cancer panic disorder) or (cancer schizophrenia) or (cancer psychotic disorder) or (cancer substance abuse) or (cancer substance dependence) or (cancer substance addiction) or (cancer personality disorder) or (cancer social work) or (cancer spiritual) or (cancer chaplain). The PubMed database was chosen because it remains the most widely used resource for medical literature, and indexes peer-reviewed biomedical literature.

The search results were narrowed by selecting studies in humans published in English. Results were confined to the following article types: Clinical Trial, Phase II; Clinical Trial, Phase III; Clinical Trial, Phase IV; Guideline; Randomized Controlled Trial; Meta-Analysis; Systematic Reviews; and Validation Studies. The data from key PubMed articles as well as articles from additional sources deemed as relevant to these guidelines as discussed by the panel during the Guidelines update have been included in this version of the Discussion section. Recommendations for which high-level evidence is lacking are based on the panel's review of lower-level evidence and expert opinion.

Sensitive/Inclusive Language Usage

NCCN Guidelines strive to use language that advances the goals of equity, inclusion, and representation. NCCN Guidelines endeavor to use language that is person-first; not stigmatizing; anti-racist, anti-classist, antimisogynist, anti-ageist, anti-ableist, and anti-weight-biased; and inclusive of individuals of all sexual orientations and gender identities. NCCN Guidelines incorporate non-gendered language, instead focusing on organ-specific recommendations. This language is both more accurate and more inclusive and can help fully address the needs of individuals of all sexual orientations and gender identities. NCCN Guidelines will continue to use the terms *men*, *women*, *female*, and *male* when citing statistics, recommendations, or data from organizations or sources that do not use inclusive terms. Most studies do not report how sex and gender data are collected and use these terms interchangeably or inconsistently. If sources do not differentiate gender from sex assigned at birth or organs



present, the information is presumed to predominantly represent cisgender individuals. NCCN encourages researchers to collect more specific data in future studies and organizations to use more inclusive and accurate language in their future analyses.

Psychosocial Problems in Adult Patients with Cancer

Dramatic advances in early detection and treatment options have increased the overall survival rates in patients of all ages with cancer. At the same time, these improved treatment options are also associated with substantial long-term side effects, such as fatigue, pain, anxiety, and depression, which interfere with patients' ability to perform daily activities. In addition, the physiologic effects of cancer itself and certain anti-cancer drugs can also be non-psychological contributors to distress symptoms.³⁻⁵ Furthermore, patients with cancer may have pre-existing psychological or psychiatric conditions that affect their ability to cope with cancer. Survivors of cancer are approximately twice as likely to report medication use for anxiety and depression as adults who do not have a personal history of cancer.⁶

Overall, surveys have found that 20% to 62% of patients show a significant level of distress.⁷⁻¹⁰ The prevalence of psychological distress in individuals varies by the type and stage of cancer as well as by patient age, gender, and race.¹¹ Further, the prevalence of distress, depression, and psychiatric disorders has been studied in many stages and sites of cancer.¹²⁻¹⁶ Cancers of the head and neck may be particularly distressing since treatment may be disfiguring and associated with impacts on essential functions such as eating, swallowing, breathing, and speaking.¹⁷ Depression is also common in pancreatic cancer, a disease often associated with a poor prognosis.¹⁸

The panel identified characteristics associated with psychosocial distress. Patients at increased risk for moderate or severe distress are those with a history of psychiatric disorder, current depression, or substance use disorder and those with cognitive impairment, severe comorbid illnesses, uncontrolled symptoms, communication barriers, prior trauma and/or abuse (physical, sexual, emotional, and/or verbal), or social issues. Social issues/risk factors include adolescence or young adulthood, recent immigration, social isolation and living alone, loss of housing or living environment, discrimination, and having young children. Patients may also experience distress about fertility and sexual health, such as loss of sexual desire and difficulty with orgasm and/or maintaining an erection.¹⁹⁻²¹ Learning about genetic/familial risk of cancer is also associated with distress.^{22,23}

Distress is a risk factor for non-adherence to cancer treatment.^{24,25} In addition to decreased adherence to treatment, failure to recognize and treat distress may lead to several problems: patients may have trouble making decisions about treatment and may make extra visits to the physician's office and emergency room, which takes more time and causes greater stress to the oncology team.^{26,27} An analysis of 1036 patients with advanced cancer showed that distress is associated with longer hospital stays (P = .04).²⁸ Distress in patients with cancer also leads to poorer quality of life and may even negatively affect survival.²⁹⁻³¹ Furthermore, survivors with untreated distress have poorer compliance with surveillance screenings and are less likely to exercise and quit smoking.³²

Early evaluation and screening for distress leads to early and timely management of psychological distress, which in turn improves medical management.³³ A randomized study showed that routine screening for distress, with referral to psychosocial resources as needed, led to lower levels of distress at 3 months than did screening without personalized triage for referrals.³⁴ Those with the highest level of initial distress benefitted the most. Overall, early detection and treatment of distress lead

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to better adherence to treatment, better communication, fewer calls and visits to the oncologist's office, and avoidance of patients' anger and development of severe anxiety or depression.

Barriers to Distress Management in Cancer

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Many patients with cancer who are in need of psychosocial care are not able to get the help they need because of the under-recognition of patients' psychological needs by the primary oncology team and lack of knowledge of community resources.³⁵ The need is particularly acute in community oncologists' practices where there are often fewer psychosocial resources.

An additional barrier to patients receiving the psychosocial care they require is the stigma associated with psychological problems. For many centuries, patients were not told their diagnosis of cancer due to the stigma attached to the disease. Since the 1970s, this situation has changed and patients are well aware of their diagnosis and treatment options.³⁶ Many patients, however, may be reluctant to reveal emotional problems to the oncologist. The words "psychological," "psychiatric," and "emotional" may be as stigmatizing as the word "cancer." The word "distress" is less stigmatizing and more acceptable to patients and oncologists, but psychological issues remain stigmatized even in the context of coping with cancer. Consequently, patients often do not tell their physicians about their distress and physicians do not inquire about the psychological concerns of their patients. The recognition of patients' distress has become more difficult as cancer care has shifted to the ambulatory setting, where visits are often short and rushed. These barriers prevent distress from receiving the attention it deserves, despite the fact that distress management is a critical component of the total care of the person with cancer.

NCCN Guidelines for Distress Management

A major milestone in the improvement of psychosocial care in oncology was made by NCCN when it established a panel to develop clinical practice guidelines, using the NCCN format. The panel began to meet in 1997 as an interdisciplinary group. The clinical disciplines involved were: oncology, nursing, social work and counseling, psychiatry, psychology, and clergy. A patient advocate was also on the panel. Traditionally, clergy have not been included on NCCN Guidelines panels, but NCCN recognized that many distressed patients prefer to speak with a certified chaplain.37

The first step was to understand why this area has been so difficult to develop. The panel members decided that words like "psychiatric" or "psychological" are stigmatizing; patients and oncologists were reluctant to label any symptoms or patients as such. The way around this barrier was developed by using a term that would feel "normal" and non-stigmatizing. This led to the first published guidelines in 1999 for the management of distress in patients with cancer. This accomplishment provided a benchmark, which has been used as a framework in the handbook for oncology clinicians published by the International Psycho-Oncology Society (IPOS) Press.38

The panel defines distress as a multifactorial, unpleasant experience of a psychological (ie, cognitive, behavioral, emotional), social, spiritual, and/or physical nature that may interfere with one's 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.

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Recommendations in the guidelines are based on evidence and consensus among panel members. In addition to the guidelines for oncologists, the panel established guidelines for social workers, certified chaplains, and mental health professionals (psychologists, psychiatrists, psychiatric social workers, and psychiatric nurses).

The New Standard of Care for Distress Management in Cancer

Psychosocial care had not been considered as an aspect of quality cancer care until the publication of a 2007 National Academy of Medicine (NAM) (formerly the Institute of Medicine) report, *Cancer Care for the Whole Patient*,³⁹ which is based on the pioneering work of the NCCN Panel. Psychosocial care is part of the standard for quality cancer care and should be integrated into routine care.³⁹⁻⁴¹ The NAM report supported the work of the NCCN Guidelines for Distress Management by proposing a model for the effective delivery of psychosocial health services that could be implemented in any community oncology practice:

- Screening for distress and psychosocial needs;
- Making and implementing a treatment plan to address these needs;
- Referring to services as needed for psychosocial care; and
- Reevaluating, with plan adjustment as appropriate.

In August 2012, the Commission on Cancer (CoC) of the American College of Surgeons (ACS) released new accreditation standards for hospital cancer programs. Their patient-centered focus now includes screening of all patients with cancer for psychosocial distress. These standards are required for accreditation, were enacted in 2015, and were updated in 2020 (<u>https://www.facs.org/quality-programs/cancer-</u> <u>programs/commission-on-cancer/standards-and-resources/</u>). According to the most up-to-date accreditation standards, institutions are expected to document and monitor their distress screening process. The standards of care for managing distress proposed by the NCCN Distress Management Panel are broad in nature and should be tailored to the particular needs of each institution and group of patients. The overriding goal of these standards is to ensure that no patient with distress goes unrecognized and untreated. The panel based these standards of care on quality improvement guidelines for the treatment of pain.⁴² The standards of care developed by the NCCN Distress Management Panel are as follows:

- Distress should be recognized, monitored, documented, and treated promptly at all stages of disease and in all settings.
- Screening should identify the level and nature of the distress.
- Ideally, patients should be screened for distress at every medical visit as a hallmark of patient-centered care. At a minimum, patients should be screened to ascertain their level of distress at the initial visit, at appropriate intervals, and as clinically indicated, especially with changes in disease status (eg, remission, recurrence, or progression; treatment-related complications).
- Distress should be assessed and managed according to clinical practice guidelines.
- Interdisciplinary institutional committees should be formed to implement standards for distress management.
- Educational and training programs should be developed to ensure that health care professionals and certified chaplains have knowledge and skills in the assessment and management of distress.
- Licensed mental health professionals and certified chaplains experienced in the psychosocial aspects of cancer should be readily available as staff members or by referral.
- Medical care contracts should include adequate reimbursement for services provided by mental health professionals.

• Clinical health outcomes measurements should include assessment of the psychosocial domain (eg, quality of life; patient and family satisfaction).

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- Patients, families, and treatment teams should be informed that distress management is an integral part of total medical care and includes appropriate information about psychosocial services in the treatment center and in the community.
- Finally, the quality of distress management programs/services should be included in institutional continuous quality improvement (CQI) projects.

Patients and families should be made aware of this standard and that it should be expected at their oncologist's practice. The website for the Alliance for Quality Psychosocial Cancer Care, a coalition of professional and advocacy organizations whose goal is to advance the recommendations from the NAM report, has hundreds of psychosocial resources for health care professionals, patients, and caregivers, and is searchable by state (https://www.cancersupportcommunity.org/alliancequality-psychosocial-cancer-care).

Recommendations for Implementation of Standards and Guidelines

A 2013–2014 survey of applicants for a distress screening cancer education program, spanning 70 institutions, showed that fewer than half of these institutions had not yet begun implementation of a distress screening program.⁴³ A 2014 survey of 55 cancer centers in the United States and Canada showed that adherence to an institution's distress screening protocol (ie, screening with appropriate documentation) occurred 63% of the time.³³ Another 2014 survey of 2134 members of the Association of Oncology Social Work (AOSW) who were also employees of a CoC-accredited cancer program showed that most programs now have procedures in place to address psychosocial care and are successful in identifying patients' psychosocial needs and appropriately addressing them.⁴⁴ However, programs tend to be less successful with follow-up of psychosocial care and training of providers regarding psychosocial care. A 2012 survey completed by 20 NCCN Member Institutions showed that most institutions do not formally keep track of the number of patients who use psychosocial care and/or services, which limits the ability to ensure that centers are adequately implementing standards of psychosocial care.⁴⁵

The MD Anderson Cancer Center published a 2010 report on its efforts to implement the integration of psychosocial care into clinical cancer care.⁴⁶ The authors outline strategies they used to accomplish the required cultural shift and describe the results of their efforts. Other groups have also described their efforts toward implementing psychosocial screening in various outpatient settings.⁴⁷⁻⁵⁵ Surveys and interviews with clinical staff have identified barriers to adoption of distress screening and have found that time, staff uncertainties, competing demands, absence of clear systematic procedures, inadequate training, and ambiguous accountability are some of the biggest barriers.⁵⁶⁻⁵⁹ A survey of oncology nurses also found that nurses who were familiar with these NCCN Guidelines for Distress Management were more comfortable discussing distress.⁵⁶

Institutions should have a framework in place to deliver psychosocial care, to effectively manage distress in patients who would benefit from psychosocial services.⁶⁰ Some initiatives have been developed to assist institutions with implementation of standards for distress screening and psychosocial care. Quality indicators can be used to determine the quality of psychosocial care given by a clinic or office. The Quality Oncology Practice Initiative (QOPI) was started in 2002 by the American Society of Clinical Oncology (ASCO) as a pilot project

(<u>http://practice.asco.org/quality-improvement/quality-programs/quality-oncology-practice-initiative</u>)⁶¹ and became available to all ASCO member

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medical oncologists in 2006. A 2008 manuscript showed that practices participating in QOPI demonstrated improved performance, with initially low-performing practices showing the greatest improvement.⁶² Blayney and colleagues from the University of Michigan Rogel Cancer Center reported that QOPI can be adapted for use in practice improvement at an academic medical center.63

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Additional guidance for the implementation and dissemination of the new NAM standards has been published. 54,60,64-71 In Canada, routine psychosocial care is part of the standard of care for patients with cancer; emotional distress is considered the sixth vital sign that is checked routinely along with pulse, respiration, blood pressure, temperature, and pain.²⁶ A national approach has been used to implement screening for distress in Canada. Its strategies have been described in the extant literature.^{72,73} Groups in Italy, France, the Netherlands, and Japan have also described results of their preliminary efforts toward the implementation of psychosocial distress screening.74-77

The panel has identified some principles of implementation to guide institutions in development of a distress screening protocol and process for appropriate referral and follow-up. These principles include the following:

- Creation of an interdisciplinary work group/committee, which ٠ ideally would include physicians, nurses, psychologists, information technology experts, social workers, chaplains, and administrative leadership
- Mandatory support from institutional leadership
- Development and execution of a pilot program prior to any largescale implementation

Consideration of the institution's already existing resources and current workflow/processes

Distress screening should be considered a measurable quality metric. Therefore, distress screening can be incorporated into institutions' quality improvement and assessment processes. Some results have caused doubt for some regarding the efficacy of distress screening for improving patient outcomes. For instance, a systematic review found no evidence that screening improved distress levels over usual care in patients with cancer.⁷⁸ Criticisms of this review include the inappropriately narrow inclusion criteria and the focus on only distress as an outcome.79 A second systematic review published in 2019, published in the Cochrane Database of Systematic Reviews, also found no evidence supporting the benefits of distress screening.⁸⁰ However, the study investigators caution that the quality of evidence is low, with more uniformity needed in outcomes and reporting. A third systematic review found that trials reporting a lack of benefit of distress screening in patients with cancer lacked appropriate follow-up care of distressed patients, while trials that linked screening with mandatory referral or intervention showed improvements in patient outcomes.81

Results of these three studies show that screening, while a critical component of psychosocial care, is not sufficient to impact patient outcomes without adequate follow-up referrals and treatment. A randomized controlled trial (RCT) examining the effects of screening on 568 patients with cancer receiving radiotherapy showed that screening alone does not significantly affect distress and quality of life, but earlier referral to mental health professionals was associated with better outcomes (ie, greater health-related quality of life, less anxiety).82 For implementation of a distress screening protocol, an ideal frequency of screening should be identified, and institutions should develop a process for generating referrals and alerting the appropriate staff based on



screening results. Whether or not screening is occurring, how often, and whether or not appropriate referrals are generated, should be tracked. This information can be used by institutions to implement improvements in the process and potentially expand needed services.

Screening Tools for Distress and Meeting Psychosocial Needs

Identification of a patient's psychological needs is essential for development of a plan to manage those needs.⁴¹ In routine clinical practice, time constraints and the stigma related to psychiatric and psychological needs often inhibit discussion of these needs. It is critical to have a fast and simple screening method that can be used to identify patients who require psychosocial care and/or referral to psychosocial resources. The NCCN Distress Management Panel developed such a rapid screening tool, as discussed below.

Screening tools have been found to be effective and feasible in reliably identifying distress and the psychosocial needs of patients.^{83,85} Completion of a psychosocial screening instrument may lead to earlier referral to social work services.⁸⁶ Mitchell and colleagues reported that ultra-short screening methods (Patient Health Questionnaire-2 [PHQ-2] or the NCCN Distress Thermometer [DT]) were acceptable to approximately three quarters of clinicians.^{87,88} Automated touch screen technologies, telephone screening, interactive voice response, and web-based assessments have also been used for psychosocial and symptom screening of patients with cancer.⁸⁹⁻⁹³

The Distress Thermometer

The NCCN Distress Management Panel developed the DT, a now wellknown tool for initial screening of 0 (no distress) to 10 (extreme distress), which is similar to the successful rating scale used to measure pain. The DT serves as an initial, single-item question screen, which identifies distress coming from any source, even if unrelated to cancer. The DT can be administered in a variety of settings, such as through a patient portal or given by a receptionist or medical assistant. If the patient's distress level is mild (score is <4 on the DT), the primary oncology team may manage the concerns with usual clinical supportive care. If the patient's distress level is 4 or higher, a member of the oncology team will use the Problem List to identify key issues of concern and ask further questions to determine the best resources (psychiatry, psychology, social work, or chaplaincy professionals) to address the patient's concerns.

The DT has been validated by many studies in patients with different types of cancer, in different settings, and in different languages, cultures, and countries. The DT has shown good sensitivity and specificity. A meta-analysis of 42 studies with greater than 14,000 patients with cancer found the pooled sensitivity of the DT to be 81% (95% CI, 0.79–0.82) and the pooled specificity to be 72% (95% CI, 0.71–0.72) at a cut-off score of 4.⁹⁴ While the DT is not a screening tool for psychiatric disorders, it has demonstrated concordance with the Hospital Anxiety and Depression Scale (HADS)⁹⁵⁻¹⁰⁴ and the Depression Anxiety and Stress Scale-21.¹⁰⁵

The NCCN DT and Problem List are freely available for non-commercial use (available at <u>www.NCCN.org</u>). In addition, the NCCN website includes a patient-friendly description of distress with a copy of the tool (<u>https://www.nccn.org/patientresources/patient-resources</u>). NCCN also has verified translations of the DT and Problem List in various languages that are freely available online (<u>https://www.nccn.org/global/what-we-do/distress-thermometer-tool-translations</u>).

The Problem List

The DT includes a 42-item Problem List, which is on the same page as the DT. The Problem List asks patients to identify their concerns in five categories: physical, emotional, social, practical, and spiritual/religious.

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The NCCN Distress Management Panel notes that the Problem List may be modified to fit the needs of the local population. Some investigators have adapted the Problem List for specific groups of patients (eg, patients with lung cancer, patients with central nervous system [CNS] tumors).^{106,107}

An analysis of the DT and Problem List including principal component analysis, logistic regression, and classification and regression tree analyses showed that endorsement of Problem List items associated with emotion (ie, sadness, worry, depression, fears, nervousness, sleep), physical function (ie, transportation, bathing/dressing, breathing, fatigue, getting around, memory/concentration, pain), and support (ie, spiritual/religious concerns, insurance/finances, dealing with partner) were significantly associated with moderate or severe distress (P < .001, P =.003, and P = .013, respectively).¹⁰⁸ Two studies validated a version of the DT with an expanded problems list.^{106, 109} Tuinman and colleagues validated the DT with the 46-item Problem List in a cross-sectional group of 227 patients with cancer.¹⁰⁹

For the 2022 Guidelines update, the panel modified the Problem List to better reflect patients' most current concerns.¹¹⁰ Specific revisions include reorganization, consolidation, and deletion of some physical concerns (eg, "bathing/dressing" and "getting around" deleted; added "loss or change of physical abilities"). Specific emotional and social concerns were added and revised (eg, combined "sadness" and "depression" into one item; added "relationship with friends or coworkers" and "communication with health care team"). Finally, specific spiritual or religious concerns were added (eg, "sense of meaning or purpose", "conflict between beliefs and cancer treatments"). The complete and up-to-date NCCN DT and Problem List are available at <u>www.NCCN.org</u>.

Cognitive Impairment

"Memory or concentration" is one item on the Problem List. Cognitive impairment is common in patients with primary CNS cancers, due to the effects of brain tumors and the effects of treatment targeted to the brain.^{111,112} Evidence has shown that chemotherapy-related cognitive dysfunction is also prevalent in patients with non-CNS cancers and without brain metastases.¹¹³⁻¹¹⁷ Chemotherapy can cause subtle cognitive changes, which have been studied primarily in patients with breast cancer or lymphoma. These changes can continue over years and at times, when more severe, can impact quality of life and function. One study, however, showed that patients with breast cancer who received systemic adjuvant therapy did not report significantly greater cognitive impairment 7 to 9 years after treatment, compared to patients with breast cancer who did not receive systemic adjuvant therapy (N = 1889), when statistically controlling for menopausal status and sociodemographic and clinical covariates.¹¹⁸ The underlying mechanisms for chemotherapy-induced cognitive changes are not known. Studies have reported elevated levels of cytokines or DNA damage as some of the possible mechanisms.¹¹⁹ Furthermore, changes in brain activity have been observed in patients following chemotherapy, suggesting that direct damage to the brain may contribute to chemotherapy-induced cognitive decline.¹²⁰

Evidence suggests that cancer and therapies other than chemotherapy, such as hormone therapy, can cause cognitive impairments in patients with cancer.¹²¹⁻¹²³ A meta-analysis including 14 studies with 417 patients with prostate cancer showed that androgen deprivation therapy negatively impacts performance of visuomotor tasks.¹²⁴ A national cross-sectional study found that a history of cancer is independently associated with a 40% increase in the likelihood of self-reported memory problems.¹²⁵ A case-control study (N = 226) showed that patients with breast cancer may experience some cognitive impairment prior to beginning treatment, and this impairment may be due to post-traumatic stress symptoms.^{126,127} A

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better understanding of the mechanisms that cause cancer-related cognitive impairment is essential for the development of treatments to improve cognitive function and quality of life in patients with cancer.^{111,112}

There is no standard treatment for the management of cognitive changes in patients with cancer, and intervention studies to date have been limited by methodologic flaws such as a small sample size, poor generalizability, and lack of a proper control group.^{115,128} Cognitive behavioral therapy (CBT), cognitive rehabilitation programs, compensatory strategy training, and exercise may be effective interventions to improve cognitive function in patients with cancer.^{115,128-132} In addition, some studies have shown that the use of psychostimulants such as methylphenidate and modafinil improved cognitive function in patients with cancer.¹³³⁻¹³⁸ Donepezil, a reversible acetylcholinesterase inhibitor (approved to treat mild to moderate dementia in patients with Alzheimer's disease) also improved cognitive function, mood, and health-related quality of life in patients with primary low-grade glioma.¹³⁹ Further placebo-controlled trials are needed to confirm these preliminary findings.^{115,134}

The NCCN Guidelines for Survivorship (available at <u>www.NCCN.org</u>) contain more information on this topic, with recommendations for the management of cognitive dysfunction in survivors.

Fertility

Another item on the Problem List is the "ability to have children." Chemotherapy and radiation therapy have an impact on the fertility of patients, especially in those who are of childbearing age.¹⁴⁰ Therefore, the panel has included "ability to have children" as one of the items listed under the family problems category. The Oncofertility Consortium is a useful patient education resource for those who are concerned about the possible effect of cancer treatment on their fertility (https://www.savemyfertility.org). Additionally, the NCCN Guidelines for Adolescent and Young Adult (AYA) Oncology (available at <u>www.NCCN.org</u>) have information on fertility and reproductive considerations.

Financial Worries

Insurance and finances are included as practical concerns in the Problem List. The impact of "financial toxicity" on cancer care is an important issue that impacts patients.¹⁴¹⁻¹⁴⁴ The cost of cancer care and diagnostic workup, as well as reduction in productivity or income due to limited ability to work, contribute to patients' concerns about financial hardship.^{141,143,145} Financial worries in cancer survivors may be more common in patients who are younger, uninsured, have a lower income, have less education, were diagnosed with late-stage or recurrent disease, or are undergoing active treatment or were treated recently.¹⁴⁴⁻¹⁴⁷ It is important for the primary oncology team to be aware of potential financial worries facing patients undergoing distress screening.

Prejudice and Discrimination

Prejudice and discrimination (eg, racism, sexism, ageism, classism, homophobia, ableism, mental illness stigma) can impact cancer care and lead to health disparities. Racial disparities have been demonstrated for guideline-concordant cancer care.^{148,149} Healthcare system factors that may lead to health disparities include differences in access to care and clinical trials and physician-patient communication, physician biases, lack of insurance or underinsurance, and other social determinants of health.^{150,151} Experiencing discrimination both in general life and in cancer care is associated with greater distress.^{152,153} Because experiences of prejudice and discrimination may contribute significantly to distress, particularly among individuals with mental illness and other groups that have been marginalized or made vulnerable, health care systems should ensure a culture of diversity, equity, and inclusiveness in the management of cancer-related distress.

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Initial Screening by Oncology Team

The panel recommends that all patients be screened prior to clinical visits using a simple tool. While there are several types of screening tools, the DT and the accompanying Problem List are recommended to assess the level of distress and to identify causes of distress. If the patient's distress is moderate or severe (DT score \geq 4), the oncology team must recognize that score as a trigger to a second level of questions, including clinical interviews and/or validated scales/screeners for anxiety and depression. A positive screen should prompt referral to a mental health professional, social worker, or spiritual counselor, depending on the problems identified in the Problem List. Common symptoms that require further evaluation are: excessive worries and fears, excessive sadness, unclear thinking, despair and hopelessness, severe family problems, social problems, and spiritual or religious concerns. Any unrelieved physical symptoms should be treated based on NCCN's disease-specific guidelines, and referral for palliative care management may also be considered (see the NCCN Guidelines for Palliative Care, available at <u>www.NCCN.org</u>).

Mild distress (DT score <4) is routinely managed by the primary oncology team and represents what the panel terms "expected distress" symptoms. The symptoms that the team manages are fear and worry about the future; concerns about the illness; sadness about loss of good health; anger and the feeling that life is out of control; poor sleep, poor appetite, and poor concentration; preoccupation with thoughts of illness, death, treatment, and side effects; concerns about social roles (eg, parent); and spiritual or existential concerns. Many patients experience these symptoms at the time of diagnosis and during arduous treatment cycles. They might persist long after the completion of treatment. For instance, minor physical symptoms are often misinterpreted by survivors as a sign of recurrence, which causes fear and anxiety until they are reassured.

The primary oncology team is the first to deal with these distressing problems. The oncologist, nurse, and social worker each have a critical role. First and foremost, a critical component is the quality of the physician's communication with the patient, which should occur in the context of a mutually respectful relationship so that the patient can learn the diagnosis and understand the treatment options and side effects. Adequate time should be provided for the patient to ask questions and for the physician to put the patient at ease. When communication is done well at diagnosis, the stage is set for future positive trusting encounters. It is important to ensure that the patient understands what has been said. Information may be reinforced with drawings or by recording the session and giving the recording to the patient. Communication skills training programs, for example, that teach oncology professionals how to discuss prognosis and unanticipated adverse events and how to reach a shared treatment decision, may be very helpful. In fact, in an RCT, it was found that patients of oncologists who had communication skills training were less depressed at follow-up than patients of oncologists from the control group (P = .027).¹⁵⁴ For a comprehensive review of communication skills training, see Kissane et al.¹⁵⁵

It is important for the oncology team to acknowledge and validate that cancer presents a unique challenge and that distress is normal and expected. Being able to express distress to the staff helps provide relief to the patient and builds trust. The team needs to ensure that social supports are in place for the patient and that the patient knows about community resources such as support groups, teleconferences, and help lines. Some selected organizations that provide free information services to patients with cancer are:

- American Cancer Society: <u>www.cancer.org</u>
- American Institute for Cancer Research: <u>www.aicr.org</u>
- American Psychosocial Oncology Society: <u>http://apos-society.org/</u>

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- Cancer Support Community: ٠ http://www.cancersupportcommunity.org (Cancer Support Community provides the Cancer Support Helpline at 888.793.9355)
- CancerCare: www.cancercare.org ٠

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- National Cancer Institute: www.cancer.gov
- Cancer.net, sponsored by ASCO: www.cancer.net

Follow-up at regular intervals or at transition points in illness is an essential part of the NCCN Guidelines for Distress Management and the NAM model for care of the whole patient.

Psychological/Psychiatric Treatment by Mental Health Professionals

Psychosocial Interventions

Psychosocial interventions have been effective in reducing distress and improving overall quality of life among patients with cancer.^{39,40} The 2007 NAM report noted that a strong evidence base supports the value of psychosocial interventions in cancer care.39 The review examined the range of interventions (psychological, social, and pharmacologic) and their impact on any aspect of quality of life, symptoms, or survival. The extensive review found randomized clinical trials, systematic reviews, and meta-analyses supporting the conclusion that psychosocial aspects must be integrated into routine cancer care to give quality cancer care. Other meta-analyses have come to similar conclusions, although more research is clearly needed.¹⁵⁶⁻¹⁵⁸ To date, psychosocial interventions for patients with cancer have disproportionately targeted women with breast cancer.^{156,157} More interventions targeting patients with other cancer types, or inclusion of mixed types, should be developed and evaluated. A metaanalysis including 53 studies of psychosocial interventions for patients with cancer (N = 12,323) showed that patients were more willing to participate in interventions delivered over the telephone versus in person (P = .031) and when intervention is offered shortly after diagnosis versus later (P =.018).¹⁵⁹ CBT, supportive psychotherapy, and family and couples therapy are three key types of psychotherapies discussed in the NAM report.³⁹

Cognitive Behavioral Therapy

CBT involves practicing relaxation techniques, enhancing problem-solving skills, and identifying and correcting inaccurate thoughts associated with feelings. In randomized clinical trials, CBT and cognitive-behavioral stress management have been shown to effectively reduce psychological symptoms (anxiety and depression) as well as physical symptoms (pain and fatigue) in patients with cancer.¹⁶⁰⁻¹⁶⁵ A Cochrane systematic review including 28 RCTs (N = 3940) showed that CBT interventions favorably address anxiety, depression, and mood disturbance in patients with nonmetastatic breast cancer.¹⁶⁶ The quality of the evidence was low for anxiety and depression and moderate for mood disturbance, however, indicating the need for studies to use higher quality intervention methods and validated instruments for measuring outcomes. Two RCTs have demonstrated improvements in distress following web-based CBT interventions.167,168

Therapy techniques rooted in CBT may be effective in reducing depression and anxiety. Behavioral activation, which is focused on decreasing avoidance and increasing engagement in activities, is associated with improvements in depression.¹⁶⁹ Some small studies have shown that behavioral activation therapy may improve depression and anxiety in patients with cancer, but larger studies are needed.^{170,171} Finally, results from small randomized trials including patients with breast cancer show that problem-solving therapy, which helps individuals focus on healthy coping methods and developing action plans to address obstacles, may improve depression in these patients.^{171,172} Another small RCT showed that problem-solving therapy reduced anxiety and distress in patients receiving hematopoietic stem cell transplant (HSCT).¹⁷³

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Supportive Psychotherapy

Supportive psychotherapy, aimed at flexibly meeting patients' changing needs, is widely used. Different types of group psychotherapy have been evaluated in clinical trials among patients with cancer. Meaning-centered group psychotherapy, designed to help patients with advanced cancer sustain or enhance a sense of meaning, peace, and purpose in their lives (even as they approach the end of life), has also been shown to reduce psychological distress among patients with advanced cancer.¹⁷⁴⁻¹⁷⁶ Dignity therapy, which has been designed for patients with a terminal diagnosis, has been evaluated in a small number of RCTs and quasi-experimental studies.¹⁷⁷ Effects on psychological well-being and quality of life are inconsistent, with additional research being needed in this area. A systematic review including six studies showed that expressive writing did not impact depression or anxiety in patients with advanced cancer.¹⁷⁸ However, the evidence was deemed low quality, and more research is needed regarding this therapeutic technique.

Interventions incorporating internet support groups have been evaluated, with a Cochrane review including six studies with 492 females with breast cancer showing a small to moderate effect on depression, based on low-quality evidence.¹⁷⁹ None of the six studies included in the review assessed emotional distress specifically, and results from two studies showed no significant effect on anxiety when comparing the intervention and control groups. Results of an RCT that included an internet support group with a prosocial component showed that this intervention did not reduce depression and anxiety in patients with nonmetastatic breast cancer (N = 184).¹⁸⁰ One systematic review showed that internet peer support interventions that are unmoderated may even be detrimental.¹⁸¹

Psychoeducation

Psychoeducational interventions are those that offer education to those with specific psychological disorders or physical conditions.

Psychoeducational interventions for patients with cancer may be general, such as providing information regarding stress management and healthy living (eg, nutrition, exercise),^{182,183} while other interventions may be more specific to the cancer type. A meta-analysis examining 19 psychoeducational interventions with 3857 patients with cancer showed small post-treatment effects overall for emotional distress, anxiety, depression, and quality of life.¹⁵⁶ The only significant effects at long-term follow-up were for guality of life. Another meta-analysis including 11 studies of psychoeducational interventions for patients with gynecologic cancers showed effectiveness for depressive symptoms.¹⁸⁴ Motivational interviewing is a patient-centered approach in which a mental health professional offers empathy as the patient explores ambivalence regarding behavior change.¹⁸⁵ One meta-analysis showed that motivational interviewing may be effective for patients with cancer for behaviors such as fruit/vegetable consumption, physical activity, smoking cessation, stress management, and sleep.¹⁸⁶ Psychoeducation interventions that offer education regarding symptom management may also be effective when delivered via the internet.^{187,188}

Family and Couples Therapy

A cancer diagnosis causes distress in partners and family members as well as the patient. Psychosocial interventions aimed at patients and their families together might lessen distress more effectively than individual interventions. In a longitudinal study of couples coping with early-stage breast cancer, mutual constructive communication was associated with less distress and more relationship satisfaction for both the patients and partners compared to demand/withdraw communication or mutual avoidance, suggesting that training in constructive communication would be an effective intervention.¹⁸⁹

Some systematic reviews have been carried out to assess the efficacy of therapy involving patients' close others. A meta-analysis including 23

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RCTs showed that patient-caregiver interventions were associated with improvements in patient quality of life, marital functioning, depression, and anxiety.¹⁹⁰ A meta-analysis focusing specifically on couple-based interventions for patients with cancer and their spouses (N = 12) showed that these interventions improved depression, anxiety, and marital satisfaction, compared to control groups.¹⁹¹ A systematic review of 23 studies that assessed the efficacy of psychosocial interventions for couples affected by cancer found evidence that couples therapy might be at least as effective as individual therapy.¹⁹² Another systematic review examining the effects of 10 interventions for couples coping with breast cancer showed that, although results are mixed, these interventions tend to yield at least some benefit.¹⁹³ A systematic review including nine studies evaluating interventions for caregiving partners of patients with cancer showed that these interventions improved caregivers' distress.¹⁹⁴ Topics covered in these partner interventions included social support, problemsolving, relationship quality, role expectations, resilience, and coping strategies. Finally, a systematic review including 11 studies evaluating interventions for family caregivers of patients with advanced cancer showed that these interventions improved caregivers' distress and caregiving burden and improved quality of life, self-efficacy, and caregiving competency.¹⁹⁵

Pharmacologic Interventions

Psychotropic medications help to manage depression and anxiety in the cancer setting. They have great benefits, as well as risks.

Antidepressants

Antidepressants help to manage both depression and anxiety in adult patients with cancer and are commonly used in these settings.¹⁹⁶⁻²⁰⁰ In RCTs, selective serotonin reuptake inhibitors (SSRIs) have efficacy in improving depressive symptoms in patients with cancer.^{201,202} Of note, antidepressants usually must be taken daily, not intermittently, and require

4 to 6 weeks to take full effect. A discontinuation syndrome of malaise, dizziness, or lightening-like pains can occur when they these medications are stopped suddenly. While not dangerous, this syndrome can be minimized by decreasing the antidepressant dose slowly over the course of weeks to months, under the supervision of a clinician. Antidepressants can sometimes interact with commonly used oncologic and other types of medications. For instance, some antidepressants prolong the cardiac QT interval and can interact with anti-cancer agents that have this same effect.

Benzodiazepines

Acute anxiety can interfere with cancer treatment (eg, anticipatory nausea and vomiting with chemotherapy; claustrophobia with radiographic assessment; anxiety exacerbating pain or sleep disturbances; anxiety impeding medical decision-making or treatment adherence; existential anxiety). Benzodiazepines, which are fast-acting, are prescribed commonly in the cancer setting for patients with acute anxiety.^{203,204} Despite their efficacy, benzodiazepines have notable risks including confusion, ataxia leading to falls and motor vehicle crashes, and addiction. Such sequelae are magnified in older adults and in patients who are frail. For these reasons, benzodiazepine use should not be undertaken lightly, and dose reduction should be considered to minimize memory difficulties, sedation, and tolerance. When used chronically, benzodiazepines should be withdrawn gradually over the course of weeks to months to avoid a withdrawal syndrome of insomnia, tremulousness, agitation, delirium, or seizures.

Antipsychotics

Antipsychotics are sometimes used in the cancer setting to manage fear, agitation, psychosis, sleep, steroid-related lability, and delirium. Risks of antipsychotics include movement disorders, restlessness, sedation, orthostatic hypotension, and asthenia. In dementia-related psychosis,



which may occur in older adult patients, antipsychotics increase the risk of death, which is noted in a black box warning. Some antipsychotics prolong the cardiac QT interval²⁰⁵ and may promote metabolic disturbance by impacting lipid metabolism.²⁰⁶

Exercise

Exercise during and after cancer treatment can improve cardiovascular fitness and strength and can have positive effects on balance, body composition, and quality of life.²⁰⁷⁻²⁰⁹ A systematic review of 20 metaanalyses showed that there was a statistically significant effect of exercise on depression in cancer survivors in 63% of the meta-analyses.²¹⁰ However, most of the effect sizes were small, with low to moderate quality of evidence. Two meta-analyses^{211,212} reported a greater pooled effect estimate for studies in which exercise took place after primary treatment was completed, compared to studies in which exercise was done during treatment. A Cochrane systematic review of patients with hematologic malignancies showed that aerobic exercise may reduce depression but not anxiety,^{213,214} while a systematic review including 12 randomized trials showed that aerobic exercise improves symptoms of both depression and anxiety in breast cancer survivors.²¹⁵ A meta-analysis examining the effects of exercise during or after chemotherapy treatment (10 studies with 838 participants) also showed an impact on depression (P = .04) but not anxiety (P > .05).²¹⁶ The quality of the evidence in this area is low, as larger RCTs and longer follow-up periods are needed. Cancer-related fatigue, which may be exacerbated by distress, is also positively impacted by exercise (see the NCCN Guidelines for Cancer-Related Fatigue, available at www.NCCN.org).^{217,218}

Complementary and/or Integrative Therapies

Regarding complementary and/or integrative therapies for patients with cancer, a systematic review showed that meditation, yoga, relaxation with imagery, massage, and music therapy may be helpful for patients with

depressive disorders who have breast cancer.^{219,220} Music therapy, meditation, and yoga may also be used to reduce anxiety in patients with breast cancer.^{219,220} A systematic review including 81 randomized and quasi-randomized trials with 5576 patients showed that music therapy benefits patients with anxiety and depression, although most of the trials included in the analysis were considered at high risk for bias.²²¹

Two meta-analyses showed that yoga may reduce depression and anxiety symptoms.^{222,223} However, the methodologic quality of the studies included in these reviews was generally low. A Cochrane review showed that, when compared to psychosocial or educational interventions, yoga may have at least short-term effects on depression (pooled standardized mean difference [SMD], -2.29; 95% CI, -3.97 to -0.61) and anxiety (pooled SMD, -2.21; 95% CI, -3.90 to -0.52).²²⁴ A systematic review showed that yoga during treatment may improve distress, but this conclusion is based on only two RCTs.²²⁵ The quality of evidence supporting yoga for symptoms of anxiety and depression is stronger for patients with breast cancer than for patients with other cancer types.²²⁶ Large randomized studies are needed to investigate the potential impact of yoga on distress.

A systematic review including 29 randomized trials showed that mindfulness-based interventions reduced anxiety, depression, and stress in patients with cancer.²²⁷ Another meta-analysis including 28 RCTs showed that these reductions in anxiety and depression persist up to 6 months after intervention.²²⁸ Meta-analyses have examined the effects of mindfulness-based stress reduction (MBSR) specifically. Two metaanalyses show that MBSR reduces distress.^{229,230} One of these analyses, which included 29 RCTs and 3274 patients showed that larger effects were found for studies that adhered to an intervention manual, included younger patients, used a passive control group, and used a shorter followup interval.²³⁰ Two meta-analyses including RCTs with patients with breast

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cancer showed that MBSR may impact anxiety and depression in the short-term only.^{231,232}

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Based on the evidence described above, the panel recommends relaxation, mindfulness, meditation, and creative therapies such as art and music for patients experiencing distress. Limitations of research in this area include inability to mask participants from the treatment they receive, lack of standardization of interventions, poor diversity of study samples, and infrequent usage of active comparator groups.²²⁶

Psychological/Psychiatric Treatment Guidelines

Patients scoring 4 or higher on the DT during any visit to the oncologist are referred to the appropriate supportive service (mental health, social work and counseling, or chaplaincy professionals) based on the identified problem. Mental health professionals are expected to conduct a psychological or psychiatric evaluation that includes an assessment of the following: the nature of the distress, changes in behavior, interpersonal problems, psychological/psychiatric history and symptoms, use of medications, substance use disorder, pain, fatigue, sleep/wake disturbances, other physical symptoms, cognitive impairment, body image, sexual health, and capacity for decision-making and physical safety. Demoralization, which is characterized by helplessness and loss of meaning and purpose, should be evaluated and distinguished from the presence of a depressive disorder.^{233,234} A psychiatrist, psychologist, nurse, advanced practice clinician, or social worker may perform the evaluation. All of these professionals are skilled in mental health assessment and treatment.

Patients with mental illness experience cancer disparities, such as increased cancer mortality rates, more advanced cancer at time of diagnosis, and more comorbidities.²³⁵⁻²³⁹ A systematic review including 13 studies showed that pre-existing severe mental illness in patients with

breast cancer is associated with less or delayed guideline-concordant care.²⁴⁰ Barriers for cancer care in patients with severe psychiatric disorders include lack of self-care, social isolation, poor adherence to medication, poor recall of medical information, interactions between cancer treatment and psychotropic medications, communication challenges, inadequate psychiatric treatment, inability to recognize signs and symptoms of cancer, stigma, fragmented care, and logistical challenges (eg, transportation difficulties).^{241,242}

The panel has developed evaluation and treatment guidelines for the most commonly encountered psychiatric disorders, consistent with the classification in the most recent edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM).²⁴³ These disorders include: neurocognitive disorders (dementia and delirium), depressive disorders, bipolar and related disorders, trauma- and stressor-related disorders (including adjustment disorders), anxiety disorders, substance-related and addictive disorders, schizophrenia spectrum and other psychotic disorders, obsessive compulsive and related disorders, and personality disorders. Psychotropic drugs are recommended throughout the guidelines to treat psychiatric disorders. It is important to note that these drugs can sometimes interact with anticancer therapies and cause adverse effects.

Patients considered to be a danger to themselves or others should be referred to psychiatry. Increased monitoring, safety planning, and removal of guns and other dangerous objects are warranted. For formal assessment of suicide risk, the Joint Commission's Suicide Prevention Recommendations should be followed

(https://www.jointcommission.org/resources/patient-safety-topics/suicideprevention/). Homicide risk evaluation may also sometimes be necessary. Directing patients to the emergency department for further psychiatric evaluation may be considered. Mental health treatment/follow-up of these

patients, family education regarding safety, and assuring the safety of others is warranted. Referral to social work, counseling, or chaplaincy care may also be considered.

Additional information regarding treatment of distress and psychiatric disorders in cancer can be found in the comprehensive handbook, *Psycho-Oncology: A Quick Reference on the Psychosocial Dimensions of Cancer Symptom Management*,²⁴⁴ and the comprehensive textbook, *Psycho-Oncology*.²⁴⁵ Additional resources targeting specific age groups include the comprehensive handbooks, *Geriatric Psycho-Oncology: A Quick Reference on the Psychosocial Dimensions of Cancer Symptom Management*,²⁴⁶ and *Pediatric Psycho-Oncology: A Quick Reference on the Psychosocial Dimensions of Cancer Symptom Management*,²⁴⁶ and *Pediatric Psycho-Oncology: A Quick Reference on the Psychosocial Dimensions of Cancer Symptom Management*,²⁴⁷ which target management of psychological, cognitive, and social difficulties in older adults and children/adolescents, respectively. The NCCN Guidelines for Supportive Care may also be referred to as needed (available at <u>www.NCCN.org</u>).

Neurocognitive Disorders

Neurocognitive disorders that may affect patients with cancer include dementia and delirium. Dementia and delirium are cognitive impairments that can severely alter the patient's decision-making capacity. Dementia is a permanent cognitive impairment. It is not a common complication of cancer treatment, but is often present in elderly patients as a comorbid condition.^{248,249} Patients living with dementia are diagnosed at a later stage of cancer, receive less treatment (including treatment of cancer-related pain), experience more complications and greater treatment burden, are associated with a greater caregiver burden for families, and have poorer survival, compared to patients without dementia.^{239,250} Dementia can be treated with cognitive rehabilitation, with or without medications, although treatment is largely behavior management.

Delirium is a short-term cognitive impairment that is very common in patients in palliative care settings.²⁵¹ Approximately one in three patients who are admitted to inpatient palliative care are delirious.²⁵¹ Risk factors for delirium include CNS tumors, toxicities from cancer treatment (eg, radiation therapy to the brain and certain chemotherapy regimens), physical complications (eg, metabolic encephalopathy, electrolyte abnormalities, dehydration), certain medications (eg, anxiolytics, opioids), and other predisposing comorbidities (eg, older age, pre-existing cognitive impairment, substance use).²⁵² A prospective case-control cohort study (N = 245) showed a significant association between benzodiazepine use and development of postoperative delirium (odds ratio [OR], 3.0; 95% CI, 1.3–6.8), with stronger associations for long-acting agents (OR, 5.4; 95% CI, 1.0–29.2) and high-dose exposure (OR, 3.3; 95% CI, 1.0–11.0).²⁵³

A prospective observational study of 243 patients with advanced cancer who presented to an emergency department at an NCCN Member Institution showed that delirium was present in 9% of all patients, but physicians correctly diagnosed delirium in only 59% of patients experiencing delirium.²⁵⁴ Additional analyses from this study showed that patients with delirium had worse overall survival and were more likely to be hospitalized, compared to patients without delirium.²⁵⁵ A retrospective chart review of 771 palliative care consultations showed that symptoms of delirium were misinterpreted by the primary oncology team 61% of the time.²⁵⁶

Delirium is usually reversible, and treatment depends on factors contributing to the patient's delirium. Delirium is managed by attention to safety, modification of opioids or other medications, antipsychotics, behavior management, and family support and education.^{257,258} The European Society of Medical Oncology has issued detailed guidelines describing diagnosis and management of delirium in patients with cancer.²⁵² In addition, a comprehensive review in *The Journal of Clinical*

Oncology Special Series on Psychosocial Care in Cancer by Breitbart and Alici²⁵⁹ describes the evidence base for recommended pharmacologic and non-pharmacologic treatments for delirium in patients with cancer.

Depressive and Bipolar-Related Disorders

Depressive and bipolar-related disorders are common in patients with cancer and can be debilitating.²⁶⁰⁻²⁶³ A cross-sectional analysis of 2141 patients with cancer showed a 4-week prevalence rate of 6.5% (95% CI, 5.5–7.5) for a depressive or bipolar-related disorder.²⁶⁴ Depressive symptoms during cancer diagnosis and treatment may persist for as long as 2 years following diagnosis.²⁶⁵ Depressive and bipolar-related disorders are associated with poorer cancer survival.²⁶⁶⁻²⁶⁸

Patients with uncontrolled depressive and bipolar-related disorders can develop suicidal tendencies. A study of more than 5000 patients at one center found that 6% of patients with cancer experienced suicidal ideation.²⁶⁹ The incidence of suicide among patients with cancer in the United States is two to three times higher than that of the general population.²⁷⁰⁻²⁷³ Older patients, patients who undergo high-morbidity surgeries, and men with head and neck cancer or myeloma seem to have a higher risk of suicide.²⁷³⁻²⁷⁶ Suicide risk in patients with cancer may be highest in approximately the first 6 months to 2 years following diagnosis.^{277,278} A large population-based cohort study including 16,771,397 patients with cancer diagnosed between 2000 and 2016 showed increased suicide risk in the first 2 years following diagnosis in those diagnosed with cancers with poor prognosis and high symptom burden (eg, cancer of the oral cavity, brain cancer, pancreas cancer).²⁷⁸ After 2 years, suicide risk is increased among those diagnosed with cancers that generally impact long-term quality-of-life (eg, leukemia, female breast cancer, uterine cancer, bladder cancer). Another retrospective cohort study of SEER data including 1,811,397 patients diagnosed with cancer between 2000 and 2016 who underwent surgical

treatment showed that suicide risk is highest in patients with cancers of the larynx, oral cavity and pharynx, esophagus, bladder, pancreas, stomach, lung, ovary, brain, colon, and rectum.²⁷⁹ Among patients with breast cancer, suicide mortality is associated with younger age, being male, non-White non-Black race, being unmarried, having undergone surgery, having progesterone-receptor—positive disease, and shorter time elapsed since diagnosis.²⁸⁰ Among patients with colorectal cancer, suicide rates were higher among males than females.²⁸¹ Violence may also be associated with depressive disorders, particularly when there is comorbid substance use.²⁸² Therefore, both suicide and homicide risk should be evaluated in patients believed to be a danger to themselves and others.

Depressive and bipolar-related disorders are usually managed with psychotherapy or psychotropic medication (category 1). The evidence for these treatments has been described.283-293 There is evidence that telehealth interventions can improve depression outcomes.²⁹⁴ Referral to social work, and counseling, as well as chaplaincy services, may also be considered. If these patients have no or only a partial response to treatment, then the chosen psychotherapeutic intervention should be reevaluated. The following options should also be considered: 1) augmenting or changing medication; 2) electroconvulsive therapy (ECT); 3) higher level care with an intensive outpatient program; and 4) reevaluation of diagnosis and treatment. In ECT, electrical currents are passed through the brain in a controlled fashion, inducing a brief seizure. ECT appears to be an effective treatment for psychotic depression, mania, catatonia, and other psychiatric disorders.²⁹⁵⁻²⁹⁸ Although the use of ECT in cancer has not been well-studied, several case studies suggest that it can be safe and effective.²⁹⁹⁻³⁰¹

ASCO has released a clinical oncology guideline adaptation of a pan-Canadian practice guideline for the screening, assessment, and treatment of anxiety and depression in patients with cancer.³⁰² The panel

recommends that a validated tool be used to screen for depressive disorders. Brief tools such as the PHQ-2 and PHQ-9 are superior to the DT for this purpose (see *Screening Tools for Distress and Meeting Psychosocial Needs: Distress Thermometer*, above).

Schizophrenia Spectrum and Other Psychotic Disorders

Psychotic disorders include hallucinations, delusions, and/or thought disorders; patients with recurrent psychotic episodes are considered to have a schizophrenia spectrum disorder. Schizophrenia spectrum and other psychotic disorders can exist as comorbidities in patients with cancer and can also be caused or exacerbated by cancer and its associated stress and treatment. In particular, corticosteroids or corticosteroid withdrawal can induce psychosis, which may be relieved by modifying dose or changing corticosteroid choice.^{303,304} When a patient in a long-term psychiatric facility develops cancer, there is a need for coordination of care between the psychiatric facility and the inpatient cancer facility. Special attention should be paid to the transition of a patient under psychiatric care who needs inpatient oncology care. The issues around continuation of psychotropic medications, when they must be stopped for surgery or chemotherapy and when they should be restarted, are important issues in total care. Evaluation for any active symptoms of psychosis should be considered when someone with a history of schizophrenia or a psychotic disorder is diagnosed with cancer.

When a psychotic episode occurs in a patient with cancer, differential diagnoses must be ruled out. Delirium is often confused with psychotic disorder and is much more common; dementia, depressive and bipolar-related disorders, and substance-related and addictive disorders should also be considered. When psychotic disorder or schizophrenia spectrum disorder is diagnosed, several interventions can be considered: 1) anti-psychotic medication; 2) medication for mood; 3) admission to a psychiatric unit/hospital; or 4) ECT for psychotic depression/mania or

catatonia. Anti-psychotics may need to be urgently administered if there is risk to self, others, or the environment.

Anxiety Disorders and Obsessive Compulsive and Related Disorders

Anxiety occurs at times in most patients with cancer.^{260,305} A crosssectional analysis of 2141 patients with cancer showed a 4-week prevalence rate of 11.5% (95% CI, 10.2–12.9) for any anxiety disorder.²⁶⁴ The diagnosis of cancer and the effects of the disease and its treatment are obvious sources of unease; however, anxiety may also be related to physiologic aspects of the medical condition (eg, hormone-secreting tumors; effects of certain types of medications [bronchodilators]; withdrawal from alcohol or narcotics; pain or some other distressing physical symptom). Anxiety may not be severe or problematic, but needs to be addressed when it becomes disruptive. After ruling out medical causes, the clinician should assess symptoms to determine the particular nature of the anxiety disorder(s). Generalized anxiety disorder is usually pre-existing and may be exacerbated by illness. Panic disorder may recur during illness in a person with previous panic symptoms. Patients with cancer may also be at increased risk of agoraphobia.³⁰⁶ Obsessivecompulsive disorder is a pre-existing disorder that results in difficulty with making decisions, ruminative thoughts about illness, and fearfulness to take medication. Some patients develop phobias of needles, hospitals, and blood or conditioned nausea/vomiting related to chemotherapy. Patients with social anxiety disorder may have difficulty communicating with medical staff.³⁰⁷ Chemotherapy-induced nausea and vomiting should be managed according to the NCCN Guidelines for Antiemesis (available at www.NCCN.org). Patients with anxiety associated with religious or spiritual concerns should be referred to chaplaincy care.

The NCCN Distress Management Panel recommends psychotherapy as a category 1 recommendation for the treatment of anxiety disorders,

including obsessive compulsive disorder, after eliminating medical causes. Treatment with an antidepressant or an anxiolytic is also recommended. If there is a response to initial treatment, follow-up should occur with the primary oncology team, primary care physician, and family/caregivers. If no response or a partial response is noted, the patient should be re-evaluated, and referral to psychiatry considered. If there is still not a complete response, then the patient should be evaluated for depression and other psychiatric comorbidity.

The evidence for the effectiveness of these treatments has been reviewed.^{39,40} In a review in *The Journal of Clinical Oncology* Special Series on Psychosocial Care in Cancer, Traeger et al³⁰⁸ give a comprehensive description of the evidence for recommended pharmacologic and non-pharmacologic treatments for anxiety in patients with cancer.

Trauma- and Stressor-Related Disorders

Trauma and stressor-related disorders that may affect patients with cancer include post-traumatic stress disorder (PTSD), acute stress disorder, and adjustment disorder. PTSD may develop after arduous cancer treatments, during a cancer treatment that triggers a traumatic memory of a past frightening event, or just from the stress of a cancer diagnosis. Survivors of cancer may continue to experience PTSD symptoms,³⁰⁹⁻³¹¹ and fear of cancer recurrence may be significant.

Reported cancer-related PTSD prevalence rates can vary, with higher rates in studies utilizing self-report questionnaires for evaluation of PTSD symptoms, compared to studies in which PTSD was evaluated with structured, clinical diagnostic interviews.³¹²⁻³¹⁴ Research on PTSD in patients with cancer largely comes from studies of white females with breast cancer.³¹³ A 2015 meta-analysis including 25 studies with 4189 cancer survivors (mostly survivors of breast cancer) showed that self-

reported PTSD symptoms occur in 7.3% of survivors, while rates based on structured clinical interviews are 12.6% for lifetime PTSD and 6.4% for current PTSD.³¹⁵ A similar 2017 meta-analysis showed that prevalence of PTSD in cancer survivors was 12.8% based on self-reported measures and 4.0% if assessed via clinical interview.³¹⁴ A 2021 meta-analysis including seven studies of patients with breast cancer showed that clinically significant PTSD symptoms were present in 31.4% of patients prior to receiving treatment.³¹⁶ A survey study including 566 survivors of non-Hodgkin's lymphoma showed that one-third reported persistent or worsening PTSD symptoms over a 5-year period.³¹⁷ Subsyndromal PTSD, in which PTSD symptoms (including impairment) are reported without meeting full diagnostic criteria, are also reported in patients with cancer.³¹⁸

Risk factors for cancer-related PTSD include: PTSD or other psychiatric diagnosis prior to cancer diagnosis; previous trauma history; lower socioeconomic status (SES); younger age at cancer diagnosis; limited social support, or perception of negative social support; low emotional selfefficacy; avoidant coping; diagnosis of advanced disease; invasive cancer treatment; dissociative symptoms relating to one's cancer experience; and persistent intrusive re-experiencing of one's own cancer experiences.^{313,315,319-329} A meta-analysis including 26 studies showed that post-traumatic stress symptoms were significantly positively associated with depression (r = 0.56), anxiety (r = 0.65), and distress (r = 0.62), and negatively associated with social support (r = -0.33) and physical guality of life (r = -0.44).³³⁰ A study including 82 patients with head and neck or lung cancer showed that elevated dissociative reactions and heightened emotional distress in the month following initial cancer diagnosis were significantly associated with cancer-related PTSD after completing treatment.³¹⁹ Another study including 352 patients with breast cancer showed a significant correlation between cancer-related traumatic stress and perceived problematic interactions with nurses and physicians (P <.01).326

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Although many patients may describe aspects of their cancer journey as "traumatic", 331, 332 the stressor criterion in the most up-to-date DSM ("exposure to actual or threatened death, serious injury, or sexual violence") is not intended to necessarily include cancer diagnosis and treatment, as meeting this criterion requires a "sudden, catastrophic event".²⁴³ Although an event in which severe complications or adverse events are experienced may qualify for this criterion, meeting additional criteria is also required. Specifically, these criteria are those relating to intrusion, avoidance, negative alteration in cognition and mood, and increased arousal and/or reactivity. Symptoms must also be present for more than 1 month, cause significant distress or impairment in functioning, and must not be attributed to effects of a substance or other medical condition. A study including 250 young adult survivors of cancer found that prevalence of qualifying traumatic event exposure was significantly lower when using the updated DSM-5 criteria, compared to DSM-IV criteria.³³³ Another study including 291 survivors of hematologic cancer also showed that cancer-related PTSD rates were lower when utilizing DSM-5 criteria, compared to DSM-IV criteria.³³² More research on PTSD diagnostic criteria from the 5th edition of the DSM in patients with cancer is needed.

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Evaluation for adjustment disorder should be done for patients who meet only some of the criteria for PTSD, if symptoms are not better explained by alternate disorders (eg, an anxiety or depressive disorder).³¹² Acute stress disorder is diagnosed in the first month following a traumatic event, and the criteria contain a greater emphasis on dissociative symptoms. Twentythree percent to 28% of patients diagnosed with cancer meet the criteria for acute stress disorder.^{325,334-337} A study of 82 patients with head and neck cancer or lung cancer showed that only 40% of patients diagnosed with acute stress disorder in the month following diagnosis met criteria for PTSD at 12-month follow-up (based on the 4th edition of the DSM), indicating that acute stress disorder may not strongly predict later diagnosis of PTSD.³²⁵ Adjustment disorder refers to a cluster of symptoms such as stress, depressive symptoms, and physical symptoms following a stressful life event such as cancer diagnosis and treatment. It may be diagnosed when a patient who experienced a stressful life event does not meet criteria for PTSD or acute stress disorder. Adjustment disorder occurs in 15.4% of patients in palliative care settings and in 11% to 19% of patients in oncologic and hematologic settings.^{264,338,339}

For the 2023 Guidelines update, the panel separated management recommendations for adjustment disorder and PTSD and acute stress disorder. Evaluation and management of these three trauma- and stressor-related disorders are the same, except the following should be considered for PTSD and acute stress disorder: evaluation, diagnostic studies, and modification of factors relating to nausea/vomiting, withdrawal states, panic attacks, hypervigilance, fears, irritability, alcohol and recreational drug use, and spiritual/religious concerns. Treatment of these disorders includes psychotherapy (category 1) with or without an antidepressant and/or an anxiolytic. If this treatment yields no response or a partial response, then psychotherapy, support, and education should be reevaluated. Choice of medication should also be reconsidered, with a consideration of antipsychotics, and referral to psychiatry should be considered. The National Cancer Institute's Physician Data Query (PDQ) provides information on cancer-related posttraumatic stress education resources that may be useful for patients (https://www.cancer.gov/aboutcancer/coping/survivorship/new-normal/ptsd-pdg) and health care professionals (https://www.cancer.gov/aboutcancer/coping/survivorship/new-normal/ptsd-hp-pdg).

Substance-Related and Addictive Disorders

Substance use and addiction are rare among patients with cancer who do not have a history of active use or addiction to opioids, alcohol, tobacco, cannabis, caffeine, or other supplements or prescription drugs. Substance use disorder developing during the course of the treatment may be due to

insufficient symptom control and can be treated by improving symptom control. Alcohol and recreational drug use should be evaluated in patients with signs and symptoms of depressive disorders, bipolar and related disorders, and anxiety disorders, as substance use may exacerbate symptoms of these disorders. Safety concerns, as well as the patient's decision-making ability, motivation to quit/cut back, and family and home environment, should be evaluated. The NCCN Guidelines for Adult Cancer Pain (available at <u>www.NCCN.org</u>) provide information on prescription, titration, maintenance, and safety of opioids. For patients who use tobacco, see the NCCN Guidelines for Smoking Cessation (available at <u>www.NCCN.org</u>).

For patients with recent problematic substance use who are motivated to quit/cut back, treatment includes referral to an outpatient substance use program, psychotherapy, and a mutual support group. Other risk reduction strategies that may be considered for these patients include psychiatric medication, medication-assisted treatment, and naloxone. If there is no response or a partial response to treatment, then referral to an intensive outpatient or residential program is recommended. Brief motivational interviewing may be done with patients who are not motivated to quit/cut back, until they are ready to do so. For patients who are currently intoxicated, alternate transportation home should be arranged, and referral to an emergency department should be considered. Patients with a history of substance use disorder should also be monitored for signs and symptoms of relapse. Relapse prevention and/or a mutual support group may also be recommended for these patients.

Personality Disorders

Patients with cancer may have a pre-existing personality disorder, which can be exacerbated by the stress of cancer and its treatment.³⁴⁰ When a personality disorder is suspected, the patient should be evaluated by a mental health professional, and safety, home situation, and decision-

making capacity should be assessed. Referral to psychiatry should be considered. If possible, any medication or other factors that could be aggravating the condition should be modified. A coordinated behavioral, psychological, and medical treatment plan, with or without medication, should be developed with the health care team.

Social Work and Counseling Services

Social work and counseling interventions are recommended when a patient has a psychosocial or practical problem. Practical problems, which may be addressed by case managers and patient navigators, are illness-related concerns; basic needs (eg, housing, food, financial/insurance concerns, help with activities of daily living, transportation); employment, school, or career concerns; cultural or language issues; and family/caregiver availability. The Guidelines outline interventions that vary according to the severity of the problem.

Common psychosocial problems are adjustment to illness; family conflicts and social isolation; difficulties in treatment decision-making; quality-of-life issues; difficulties with transitions in care; absent or unclear advance directive or other concerns about advance directives; domestic abuse and neglect; poor coping or communication skills; concerns about functional changes (eg, body image, sexual health); depressive symptoms and/or suicidal ideation; fears, nervousness, and worry; and issues pertaining to end of life and bereavement (including cultural and caregiver concerns).

Social work and counseling interventions for psychosocial problems are described in the Guidelines. Social workers intervene in mild psychosocial problems by using patient and family education, support groups, and/or sexual health or grief counseling and by suggesting available local resources. Social workers can also help foster healthy coping strategies, such as problem solving, cognitive restructuring, and emotional regulation.³⁴¹ For moderate to severe psychosocial problems, counseling

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and psychotherapy are used (including sexual health and grief counseling); community resources are mobilized; problem solving is taught; and advocacy, education, and protective services are made available.

Spiritual and Chaplaincy Care

Religiousness and spirituality are positively associated with mental health in patients with cancer,³⁴² and attendance at religious services is associated with lower cancer-related mortality.343 Many patients use their religious and spiritual resources to cope with illness,³⁴⁴ and many cite prayer as a major help. In addition, the diagnosis of cancer can cause an existential crisis, making spiritual support of critical importance. Balboni et al³⁴⁵ surveyed 230 patients with advanced cancer treated at multiple institutions who did not respond to first-line chemotherapy. The majority of patients (88%) considered religion as somewhat or very important. Nearly half of the patients (47%) reported receiving very minimal or no support at all from their religious community, and 72% reported receiving little or no support from their medical system.³⁴⁵ Importantly, patients receiving spiritual support reported a higher quality of life. Religiousness and spiritual support have also been associated with improved satisfaction with medical care. Astrow et al³⁴⁶ found that 73% of patients with cancer had spiritual needs, and that patients whose spiritual needs were not met reported lower quality of care and lower satisfaction with their care. A multi-institution study of 75 patients with cancer and 339 oncologists and nurses (the Religion and Spirituality in Cancer Care Study) found that spiritual care had a positive effect on patient-provider relationships and the emotional well-being of patients.³⁴⁷ However, a survey conducted in 2006 through 2009 found that most patients with advanced cancer never receive spiritual care from their oncology team.³⁴⁸ Spiritual needs may include searching for the meaning and purpose of life; searching for the meaning in experiencing a disease like cancer; being connected to others, a deity, and nature; maintaining access to religious/spiritual practices;

spiritual well-being; talking about death and dying; making the most of one's own life; and being independent and treated like a "normal person."³⁴⁹

Multiple meta-analyses show that spiritual interventions improve quality of life, as well as depression and anxiety, although effects may be small, and included studies in these reviews are often varied in their design.³⁵⁰⁻³⁵² A meta-analysis including 24 studies showed that existential interventions positively affected existential well-being, quality of life, hope, and self-efficacy, although results were moderated by interventional characteristics (eg, therapist's professional background, intervention setting).³⁵³

The panel has included chaplaincy care as part of psychosocial services. All patients should be referred to a chaplaincy professional when their problems are spiritual or religious in nature or when they request it. Guided by the Religious and Spiritual Struggles Scale³⁵⁴ and the Existential Concerns Questionnaire,³⁵⁵ the panel identified issues that should be included as part of evaluation by a chaplain: interpersonal conflict regarding spiritual/religious beliefs and practices; concerns with lack of meaning and purpose; struggles with morality and values; doubts about beliefs; perceptions of being attacked by evil; preoccupation about religiosity; issues of forgiveness; concerns about one's relationship with the sacred; concerns about death, dying, and the afterlife; grief and loss; feeling worthless or like a burden; loneliness; conflict between religious beliefs and treatment options; and ritual needs.

The panel has identified interventions that may be carried out based on this assessment. These interventions, which are based on recommendations by Spiritual Health Victoria

(<u>https://www.spiritualhealth.org.au/standards</u>), include spiritual/existential counseling, education, and rituals; meditation and/or prayer; referral to appropriate spiritual/existential community resources; and referral to other

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health care professionals (eg, palliative care, mental health professional) as needed.

The following guidelines on religion and spirituality in cancer care may also be useful for clinicians and patients:

• National Consensus Project Clinical Practice Guidelines for Quality Palliative Care, Fourth Edition, 2018

(<u>https://www.nationalcoalitionhpc.org/ncp/</u>). These guidelines provide a framework to acknowledge the patient's religious and spiritual needs in a clinical setting. Spiritual, religious, and existential aspects of care are included as 1 of the 8 clinical practice domains.

 The National Cancer Institute's comprehensive cancer information database (PDQ) has information on "Spirituality in Cancer Care" for patients

(<u>http://www.cancer.gov/cancertopics/pdq/supportivecare/spirituality/Patient)</u> and for health care professionals

(<u>http://www.cancer.gov/cancertopics/pdq/supportivecare/spirituality/Heathertopics/pdq/supportivecare/spirituality/Heathertopics/pdq/supportivecare/spirituality/Heathertopics/pdq/supportivecare/spirituality/Heathertopics/pdq/supportivecare/spirituality/Heathertopics/pdq/supportivecare/spirituality/Heathertopics/pdq/supportivecare/spirituality/Heathertopics/pdq/supportivecare/spirituality/Heathertopics/pdq/supportivecare/spirituality/Heathertopics/pdq/supportivecare/spirituality/Heathertopics/pdq/supportivecare/spirituality/Heathertopics/spirituality/Heath</u>

Oncologist Burnout

The stress and demands of treating patients with cancer and making life and death decisions daily often cause psychologic distress for oncologists. This distress can in turn cause depression, anxiety, and fatigue. It can also cause moral distress, compassion fatigue, and/or burnout. Burnout, characterized by a lack of enthusiasm for work, feelings of cynicism, and a low sense of personal accomplishment with work, occurs in as many as 28% to 45% of oncologists.³⁵⁶⁻³⁵⁹ Burnout can affect patient care, physician-patient relationships, and personal relationships and can lead to substance use disorder and even suicide. Strategies for avoiding and reducing burnout include training in self-care, personal wellness, and mindful meditation, and behavioral change by medical schools, residency programs, hospitals, and private practices.^{356,360} Organizational strategies can also create a culture that is less stressful and less conducive to oncologist burnout.

Summary

Psychosocial care is an integral component of the clinical management of patients with cancer. The CoC's accreditation standards include distress screening for all patients and referral for psychosocial care as needed. Screening for and treating distress in cancer benefits patients, their families/caregivers, and staff and helps improve the efficiency of clinic operations. For patients with cancer, integration of mental health and medical services is critically important. Spirituality and religion also play an important role in coping with the diagnosis and the illness for many patients with cancer.

The NCCN Guidelines for Distress Management recommend that each new patient be rapidly evaluated in the office or clinic waiting room for evidence of distress using the DT and Problem List as an initial global screen. A score of 4 or greater on the DT should trigger further evaluation by the oncologist or nurse and referral to an appropriate resource, if needed. The choice of which supportive care service is needed is dependent on the problem areas specified on the Problem List. Patients with practical and psychosocial problems should be referred to social work and counseling services; those with emotional or psychological problems should be referred to mental health professionals; and spiritual concerns should be referred to chaplaincy care. Physical concerns may be best managed by the medical team.

Education of patients and families regarding distress is important, and they should be encouraged to recognize that controlling distress is an integral part of their total cancer care. The patient version of the NCCN Guidelines for Distress Management is a useful tool to accomplish this (https://www.nccn.org/patientresources/patient-resources).

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