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## Survivorship, Version 1.2016:

### Featured Updates to the NCCN Guidelines

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## Abstract

The NCCN Guidelines for Survivorship provide screening, evaluation, and treatment recommendations for common consequences of cancer and cancer treatment. They are intended to aid health care professionals who work with survivors of adult-onset cancer in the posttreatment period, including those in general oncology, specialty cancer survivor clinics, and primary care practices. Guidance is also provided to help promote physical activity, weight management, and proper immunizations in survivors. This article summarizes the NCCN Survivorship panel's

discussions for the 2016 update of the guidelines regarding the management of anxiety, depression, posttraumatic stress disorder–related symptoms, and emotional distress in survivors.

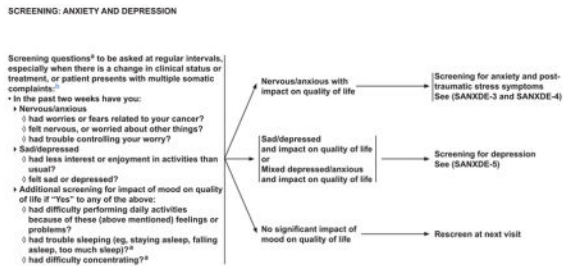
**GENERAL PRINCIPLES OF ANXIETY, DEPRESSION, AND DISTRESS**

- The NCCN Guidelines for Distress Management define distress as “a multifactorial unpleasant emotional experience of a psychological (ie, cognitive, behavioral, emotional), social, and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms, and its treatment.”
- Survivors of cancer treatment are at high risk for fear of recurrence, distress, anxiety, and depression due to the multiple challenges they face.
  - Fear of recurrence can lead to increased symptoms when surveillance testing or follow-up appointments are scheduled and increased anxiety when physical symptoms occur that may or may not be similar to those experienced during the cancer diagnosis.
  - Medical, psychosocial, environmental, and psychiatric health factors may affect the mood of cancer survivors and need to be considered when screening for distress, anxiety, and depression in survivors and deciding on treatment. (See SANKDE-4)
  - Recurrent worry, fear, thoughts, or images related to cancer events should be distinguished from obsessive compulsive disorders. Repetitive, persisting thoughts, images, or behaviors or mental acts that a person is compelled to perform, aimed at reducing intense anxiety or preventing a dreaded event requires psychiatric referral for evaluation and treatment.
  - Monitor distress, especially at times of transitions in care, cancer surveillance, significant loss, other major life events, and with social isolation.
  - Patients may not appear to be distressed and should be encouraged to inform their health care provider when they are feeling increased distress, anxiety, or depression. See DIS-8 from the NCCN Guidelines for Distress Management.
- This algorithm is intended for oncologists and other health care providers to screen for distress, anxiety, and depression in cancer survivors, to provide steps for addressing these concerns with survivors, and to facilitate decisions about referral to specialists.
  - The algorithm is not intended as a psychiatric diagnosis and treatment tool.
  - The algorithm focuses on more common mood disorders after cancer; it does not screen or address treatment for psychiatric conditions such as bipolar disorders, schizophrenia, personality disorders, or obsessive compulsive disorders.
- Decisions about treatment and referral will depend on the acuteness of onset of symptoms, their intensity, and safety of the survivor and others. (See SANKDE-6 and SANKDE-A)

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### Overview

Nearly 14.5 million cancer survivors were alive in the United States in 2014, and these numbers are predicted to reach almost 19 million by 2024.<sup>1,2</sup> Unfortunately, many of these survivors experience physical (eg, fatigue, pain, lymphedema, premature menopause, cognitive deficits, sexual dysfunction), psychological (eg, anxiety, depression, fear of recurrence), and psychosocial (eg, issues surrounding employment, finances, insurance) late and long-term effects of cancer and its treatment.<sup>3–22</sup> These effects can be severe, debilitating, and sometimes permanent or life-threatening. Survivors may be discharged from the care of their oncologist or see the oncology team less frequently, resulting in feelings of isolation and worry or fear. Furthermore, their primary care physicians (PCPs), who may now be responsible for their care, often do not know how best to care for the specific concerns and needs of cancer survivors.<sup>23</sup>



\*A positive response to any of the questions should result in further assessment. However, if a patient has an isolated problem with sleep or concentration in the absence of other symptoms, refer to the Sleep Disorders Guidelines (SDS-1) or Cognitive Function Guidelines (CF-1).  
<sup>†</sup>If the NCCN Distress Thermometer is used as a primary screening tool, these questions would follow for those survivors with an elevated level of distress.  
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The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Survivorship aid health care professionals who work with survivors of adult-onset cancers in the posttreatment period by providing screening, evaluation, and treatment recommendations for common consequences of cancer and cancer treatment. The guidelines are designed to provide a framework for the management of long-term and/or late effects of cancer and its

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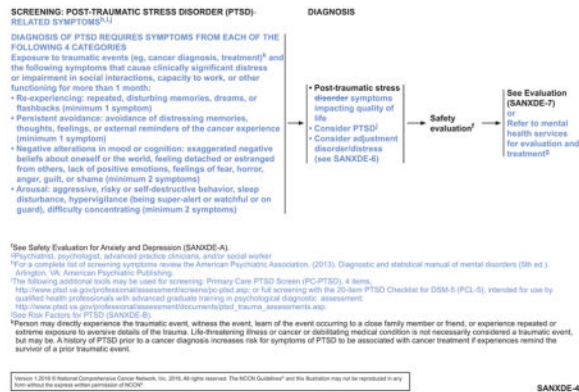
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treatment and for the coordination of care between the survivor’s health care providers to ensure that needs are appropriately addressed. They should be used as a supplement to the follow-up recommendations within the disease-specific guidelines (see NCCN Guidelines for Treatment of Cancer by Site, available at [www.NCCN.org](http://www.NCCN.org)).

The 1.2016 version of the NCCN Guidelines for Survivorship focuses on several common issues of survivors: anxiety/depression/distress; anthracycline-induced cardiac toxicity; cognitive decline; fatigue; pain; female and male sexual dysfunction; sleep disorders; and the preventive health issues of immunizations and prevention of infections and healthy lifestyle behaviors. Additional topics will be addressed in subsequent updates.

### 2016 Updates to the NCCN Guidelines for Survivorship

During the update of the NCCN Guidelines for Survivorship this year, an emerging theme highlighted the fact that clinicians may not have the expertise needed to help survivors with the wide range of possible issues they may face. The panel therefore added the option for early referral to the appropriate specialist in many cases (eg, sexual dysfunction, sleep disorders). Thus, the algorithm for many of the survivorship topics now first includes information designed to increase clinician awareness of the issues, then includes appropriate screening questions or tools followed by the option for early referral to the appropriate specialist. In addition, the guidelines provide guidance for appropriate evaluation, treatment, and follow-up care at a level that can be appropriately performed by the oncologist, PCP, or specialist.



This paradigm was used in the redesign of the section on anxiety and depression in cancer survivors, as discussed herein. Additional issues discussed by the panel this year regarding the management of anxiety, depression, posttraumatic stress disorder (PTSD)–related symptoms, and distress in survivors are also described. Changes to the guidelines are indicated with blue font in the figures.

### Anxiety, Depression, and Distress in Survivors

Cancer survivors are at especially high risk for anxiety, depression, and other forms of psychosocial distress because of the multiple stressors, vulnerabilities, and challenges they face. According to the NCCN Guidelines for Distress Management (available at

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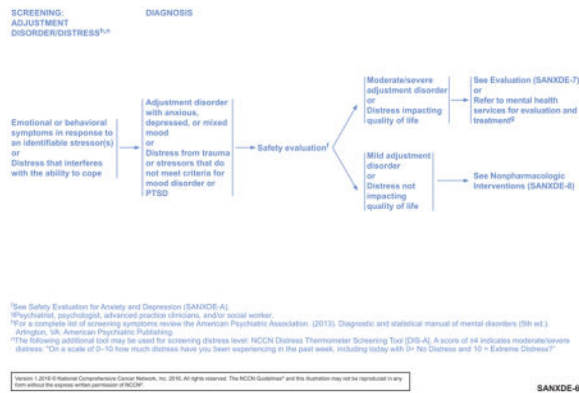
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www.NCCN.org), risk factors for psychosocial distress include cognitive impairment, severe comorbid illnesses, uncontrolled symptoms, communication barriers, or a history of psychiatric disorder, depression, or substance abuse. Social issues, such as living alone, having young children, being of younger age or female, and prior physical or sexual abuse, are also risk factors for psychosocial distress.

Fear of recurrence, with persisting worry and distress sometimes reaching levels of clinical anxiety, is common in cancer survivors. This fear can increase at times of routine cancer surveillance testing or with physical symptoms that may or may not be related to the cancer diagnosis.<sup>11,24–27</sup> Anxiety and/ or depression can also occur in survivors secondary to physical compromise, social isolation, or work and financial problems that result from cancer treatment.<sup>11,15,16,19,26</sup> These challenges are underscored by the inevitable decreased medical and interpersonal support after completion of treatment and transition to the surveillance stage.<sup>28</sup>

Anxiety and depression affect up to 29% of survivors, with 1% to 19% of survivors reportedly meeting the criteria for PTSD.<sup>11,15,29–31</sup> In addition, many survivors have less severe distress that might not lead to a clinical diagnosis of anxiety, depression, or PTSD but that can still have a negative impact on quality of life. Survivors with untreated, uncontrolled emotional distress are less likely to adhere to recommended surveillance and are less likely to engage in health-promoting activities, such as exercise and smoking cessation.<sup>32</sup> Sometimes these individuals develop thoughts of ending their lives; the incidence of completed suicide among patients with cancer and survivors in the United States is approximately twice that of the general population.<sup>33–38</sup>



**Possible Early Referral for Survivors With Anxiety, Depression, PTSD-Related Symptoms, and Distress**—Reviewers from several NCCN Member Institutions indicated that the original anxiety and depression section of the guidelines was too complex, detailing evaluation and management that were beyond the scope of the typical oncologist or PCP. The extensive evaluation was viewed as a diagnostic evaluation better performed by a trained mental health provider.

Oncologists on the panel agreed that they do not feel comfortable diagnosing major psychiatric disorders, nor should oncologists or PCPs be doing so. However, the panel discussed the pervasiveness of psychosocial problems in survivors and the fact that many

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distressed survivors may not appear distressed. The panelists strongly believe that oncologists and PCPs need to know how to screen, when to screen, and to whom to refer when screening indicates a need for services. The panel therefore added information on the prevalence of and risk factors for distress in survivors (see SANXDE-1; page 717) and modified their recommendations to include the following general structure: screening, flagging those in need of referral, ensuring the safety of the survivor, and the option for early referral to mental health services (ie, psychiatrist, psychologist, advanced practice clinicians, and/or social worker) (see SANXDE-4 and SANXDE-6 as examples; pages 717 and 718). The panel’s intent is to provide information to facilitate decisions about referrals, and to take initial steps in providing care rather than to provide guidelines for psychiatric diagnoses. Instead of specifying the full diagnostic criteria for issues such as depression, anxiety, and PTSD, the panel listed the essential criteria for screening psychiatric diagnoses that are most common in survivors, and some key symptoms from the *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition; DSM-V).<sup>39</sup>

- RISK FACTORS FOR PTSD**
- Physical
    - Recurrence of cancer
    - Intensive treatment (eg, bone marrow/stem cell transplant)
    - Advanced disease
    - Younger age
  - Psychosocial
    - Exposure to previous trauma (eg, combat, sexual assault, major loss)
    - History of mental health issues prior to cancer
    - Poor coping skills (eg, using avoidance)
    - Lower income and/or less education
    - Less social support

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SANXDE-8

The panel then discussed the fact that survivors with few or mild symptoms may be managed with oncology or primary care support and access to online, telephone-based, or community support resources, and may not require a referral to mental health services, and that in some places (eg, rural areas) there may not be sufficient mental health resources available to refer all survivors in need. It is important for oncology and PCPs to have awareness of the prevalence of anxiety, depression, and distress in survivors and guidance regarding initial steps in management. In addition, the panelists felt that guidance for the psychiatrists, psychologists, advanced practice clinicians, social workers, and/or licensed therapists who work with survivors was needed. The panel therefore retained the evaluation and management recommendations listed in the guidelines.

**Screening**—During the panel’s discussion regarding the appropriate initial screening for anxiety and depression in survivors, a panel member brought up the role of the NCCN Distress Thermometer (DT) in survivors. Several panel members noted that their institutions are using the DT to screen for distress in survivors at this time. The DT is embedded into many commercially available electronic health record (EHR) systems and is therefore used by many hospitals, clinics, and private practices.

The panel discussed the literature addressing the validity of the DT in cancer survivors. Studies generally do not support its use in a clinical survivorship setting because it lacks



sufficient sensitivity and specificity in this population.<sup>40–46</sup> For example, a study of 120 survivors of adult-onset cancer found that the DT had a sensitivity of 47.6% and 51.7%, using cutoff values of 5 and 4, respectively.<sup>44</sup>

The panel therefore recommended supplemental screening when the DT is used as an initial screening tool. They added a footnote indicating that survivors with an elevated level of distress by the DT should still be asked the initial screening questions provided by the panel (see SANXDE-2, page 718). These more specific questions allow the clinician to determine what particular issues are affecting the survivor and may identify more distressed or depressed survivors than the DT.

**Distress/Adjustment Disorder**—Reviewers from NCCN Member Institutions commented that the guidelines seemed mainly to address severe or extreme cases of anxiety and depression, but gave little guidance for cases of mild to moderate symptom burden, which are most common. Reviewers also suggested combining “mild adjustment disorder with depressed mood or with mixed depressed mood and anxiety” with “adjustment disorder with anxious mood,” noting that no clinical reasons justified their separation within the guidelines.

The panel agreed with these points. Panelists noted that many survivors may not have clinical diagnoses but still have symptoms that require further evaluation and intervention. Such survivors have what the NCCN Guidelines for Distress Management (available at [www.NCCN.org](http://www.NCCN.org)) define as distress: “a multifactorial unpleasant emotional experience of a psychological (ie, cognitive, behavioral, emotional), social, and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms, and its treatment.” Distress, often related to fear of recurrence, is common in survivors, and can negatively impact quality of life.<sup>11,24–27</sup>

The panel decided to restructure the guidelines to include a page for all survivors with symptoms who do not meet the diagnostic criteria for anxiety or depression and who do not have PTSD symptoms impacting quality of life (see SANXDE-6; page 720). This page addresses what the panel termed “adjustment disorder/distress.” To emphasize the importance of treating distress, the panel also changed the title of this section of the guideline to include the word “distress.”

**PTSD-Related Symptoms**—A panel member asked the panel to discuss PTSD, noting that, as with distress, many survivors may not meet the full diagnostic criteria for PTSD but still have PTSD-related symptoms that need to be addressed. However, the way the guideline was originally written only allowed for patients to be treated if they had full PTSD. The panel discussed various studies showing that 17% to 38% of survivors have PTSD symptoms, whereas 1% to 19% meet the full criteria.<sup>11,29,31,47–50</sup> In one longitudinal study, 12% of survivors reported that their PTSD symptoms resolved over 5 years, whereas 37% reported that their symptoms persisted or worsened during that time.<sup>30</sup> Panel members also pointed out that PTSD symptoms in survivors can fluctuate over time, because of other events or other trauma occurring in the survivor’s life.

The panel decided to expand the section on PTSD, changing it to “PTSD-related symptoms” to emphasize the fact that survivors may not meet the full diagnostic criteria for PTSD but still have symptoms deserving of treatment (see SANXDE-4, page 719). The panel included an extensive list of PTSD criteria, so that clinicians can be aware when a survivor might have PTSD. The panel also decided to add a list of risk factors for PTSD, so that clinicians are alert to the disease-related and other physical and psychosocial factors that can play a role in the disorder (see SANXDE-B, page 721). In addition, the guidelines now allow for further evaluation, referral, and treatment for survivors with PTSD-related symptoms impacting quality of life, even if the full PTSD diagnostic criteria are not met.

## Conclusions

The diagnosis and treatment of cancer can have a vast and persistent impact on the survivor’s health, physical, and mental states; health behaviors; professional and personal identity; sexuality; and financial standing. Clinicians providing survivorship care can improve the lives of the survivors by understanding this impact; conducting screening for physical, psychological, and psychosocial effects; and providing appropriate referrals, treatment, and/or follow-up. As the number of survivors continues to grow, clinician awareness about these critical issues becomes increasingly important. In particular, clinicians who work with cancer survivors need to be aware that distress is prevalent in the survivor population and may not be evident in an individual survivor without appropriate screening. Distressed survivors may not meet criteria for a full clinical psychiatric diagnosis, but can still benefit from interventions to improve quality of life. Clinicians can refer distressed survivors to an appropriate mental health professional or can perform evaluation and treatment as their expertise and resources allow.

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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.