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## Palliative Care, Version 2.2021:

### Featured Updates to the NCCN Guidelines

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### Abstract

Palliative care has evolved to be an integral part of comprehensive cancer care with the goal of early intervention to improve quality of life and patient outcomes. The NCCN Guidelines for Palliative Care provide recommendations to help the primary oncology team promote the best quality of life possible throughout the illness trajectory for each patient with cancer. The NCCN Palliative Care Panel meets annually to evaluate and update recommendations based on panel members’ clinical expertise and emerging scientific data. These NCCN Guidelines Insights summarize the panel’s recent discussions and highlights updates on the importance of fostering adaptive coping strategies for patients and families, and on the role of pharmacologic and non-pharmacologic interventions to optimize symptom management.

**Definition of Palliative Care<sup>3,6</sup>**  
 Palliative care is an approach to patient/family/caregiver-centered health care that focuses on optimal management of distressing symptoms, while incorporating psychosocial and spiritual care according to patient/family/caregiver needs, values, beliefs, and cultures. The goal of palliative care is to anticipate, prevent, and reduce suffering; promote adaptive coping; and support the best possible quality of life for patient/families/caregivers, regardless of the stage of the disease or the need for other therapies. Palliative care can begin at diagnosis; be delivered concurrently with disease-directed, life-prolonging therapies; and facilitate patient autonomy, access to information, and choice. Palliative care becomes the main focus of care when disease-directed, life-prolonging therapies are no longer effective, appropriate, or desired. Palliative care should be provided by the primary oncology team and augmented as needed by collaboration with an interprofessional team of palliative care experts.

**Standards of Palliative Care<sup>4,6</sup>**  
 • Institutions should develop processes for integrating palliative care into cancer care, both as part of usual oncology care and for patients with specialty palliative care needs.  
 • All cancer patients should be screened for palliative care needs at their initial visit, at appropriate intervals, and as clinically indicated.  
 • Patients/families/caregivers should be informed that palliative care is an integral part of their comprehensive cancer care.  
 • Educational programs should be provided to all health care professionals and trainees so that they can develop effective palliative care knowledge, skills, and attitudes.  
 • Palliative care specialists and *interprofessional palliative care teams*, including but not limited to board-certified palliative care physicians, advanced practice nurses, physician assistants, nurses, dietitians, social workers, chaplains, and pharmacists, should be readily available to provide consultative or direct care to patients/families/caregivers and/or health care professionals who request or require their expertise.  
 • Quality of palliative care should be monitored by institutional quality improvement programs.

<sup>3</sup>Hui D, et al. *J Pain Symptom Manage* 2012;43:582-592.  
<sup>4</sup>Seaman JB, et al. *J Palliat Med* 2020;23:1157-1158.  
<sup>5</sup>Frens PD, et al. *J Clin Oncol* 2020;37:3055-3056.  
<sup>6</sup>IGM (Institute of Medicine). 2014 *Dying in America: Improving quality and honoring individual preferences near the end of life*. Washington, DC: The National Academies Press. Available at: [www.nap.edu/read/13743/chapter/1](http://www.nap.edu/read/13743/chapter/1).  
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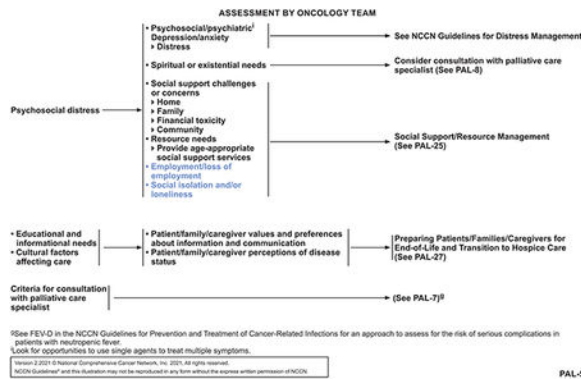
### Overview

More than 1.8 million people are expected to be diagnosed with cancer in the United States in 2021, and 608,570 people are expected to die of the disease.<sup>1</sup> Global cancer rates are increasing, with an associated rise in the number of cancer survivors living with

symptoms and disabilities as a result of their disease and/or its treatment.<sup>1-3</sup> More than one-third of patients with cancer in a large observational cohort study reported moderate to severe symptoms in most categories (pain, nausea, anxiety, depression, shortness of breath, drowsiness, well-being, loss of appetite, and tiredness) in the last weeks of life.<sup>4</sup> Several groups, including the WHO, ASCO, and American Society of Hematology, recommend integrating palliative care with disease-directed care beginning at the time of diagnosis.<sup>5-7</sup> This allows for more holistic and timely identification of challenges facing patients and their families, and more robust and restorative problem-solving.

## Palliative Care in Oncology

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) define palliative care as an approach to patient/family/caregiver-centered healthcare that focuses on optimal management of distressing symptoms, while incorporating psychosocial and spiritual care according to patient/family/caregiver needs, values, beliefs, and cultures. The goal of palliative care is to anticipate, prevent, and reduce suffering; promote adaptive coping; and support the best possible quality of life (QoL) for patients/families/caregivers, regardless of the stage of the disease or the need for other therapies. Palliative care should begin at diagnosis; be delivered concurrently with disease-directed, life-prolonging therapies; and facilitate patient autonomy, access to information, and choice. The value of early integration of palliative care into the continuum of cancer care has been well demonstrated.<sup>8-12</sup> During the recent meeting to discuss updates to the NCCN Guidelines for Palliative Care, the panel highlighted the importance of applying palliative care practices in a way that includes not only the patient but also families and caregivers. In particular, the panel stressed that the promotion of adaptive coping strategies (defined as problem-solving strategies as opposed to avoidant coping strategies) for patients, families, and caregivers should be a component of all stages of the care plan. A recent study examining patients' perception of treatment goals showed that patients who acknowledged the incurable nature of their disease reported higher psychologic distress compared with those who perceived their treatment goals as curative, regardless of accuracy of the perception.<sup>13</sup> Additionally, patients whose treatment goals were discordant with their oncologist's also reported increased distress symptoms.<sup>13</sup> In contrast, another study showed that patients with an accurate understanding that their disease was incurable who engaged in specific active coping strategies had fewer depressive symptoms than those not engaged in coping strategies.<sup>14</sup> The panel recommends encouraging adaptive coping methods for patients, family, and caregivers, particularly when cultivating prognostic awareness to help improve both goal-concordant care and QoL.



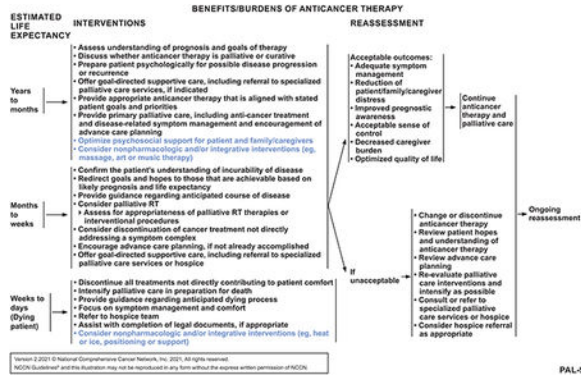
Palliative care should be initiated by the primary oncology team and should be augmented through collaboration with palliative care specialists in an interprofessional team (including but not limited to board-certified palliative care physicians, advanced practice providers, nurses, dietitians, social workers, psychologists, psychiatrists, chaplains, and pharmacists) to address intractable symptoms and/or complex psychosocial issues.<sup>15</sup> Additionally, palliative care should reach beyond the patient to include family and caregivers. During the recent meeting to discuss updates to the NCCN Guidelines, the panel acknowledged that palliative care is a collaborative practice, and therefore recommends recognition of all expertise with the term “interprofessional.” Using language that allows for a better understanding of expectations can improve teamwork during interactions among multiple areas of practice.<sup>15</sup>

## Comprehensive Assessment

Patients should undergo a comprehensive palliative care assessment by their primary oncology team, including an evaluation of the benefits and burdens of anticancer therapy; the patient’s and family’s decision-making style and capacity; their coping strategies; any physical symptoms; psychosocial or spiritual distress; personal goals, values, and expectations; educational and informational needs; potential financial toxicity; and cultural factors affecting care.<sup>16-18</sup>

## Assessment of Psychosocial Distress

Assessment of psychosocial distress should include both the patient and the caregivers, and should focus on illness-related distress and psychosocial, spiritual, or existential needs according to the NCCN Guidelines for Distress Management (available at NCCN.org). Concerns regarding social support and resources (ie, home, family, community, or financial) must also be assessed. While discussing recent updates to the Guidelines, the panel emphasized the effect that employment or the loss of employment may have on psychologic distress. Loss of employment, in particular, may lead to decreased feelings of personal purpose, increased social isolation (or loneliness) due to loss of one’s workplace community, as well as financial toxicity.<sup>19</sup> Interventions that may help to reverse some of this distress include but are not limited to promotion of adaptive coping methods for both patients and caregivers, and provision of additional psychologic and financial support, when possible (see PAL-5, page 783).

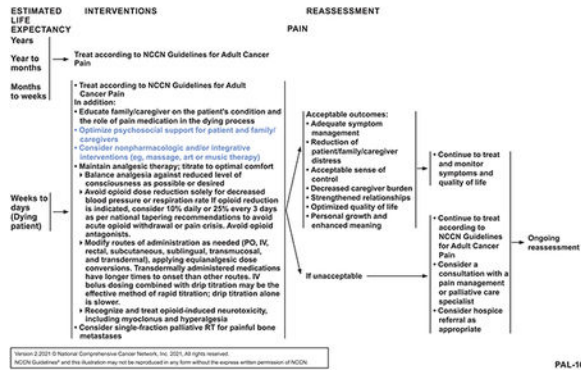


### Palliative Care Interventions

The oncology team should initiate treatments following the specific recommendations described in these guidelines for common symptoms. Comorbid physical and psychosocial conditions should be treated by appropriate clinicians. Consultation or collaboration with palliative care specialists or teams is recommended for patients with more complex concerns to improve their QoL.<sup>20-23</sup> Referrals should be made as needed to mental health, social and psychosocial support services, spiritual care, healthcare interpreters, hospice services, financial counselors, or other specialists. Finally, the oncology team may find collaboration with a palliative care team helpful in identifying additional support through religious organizations, schools, or other agencies in the community.

### Anticancer Therapy

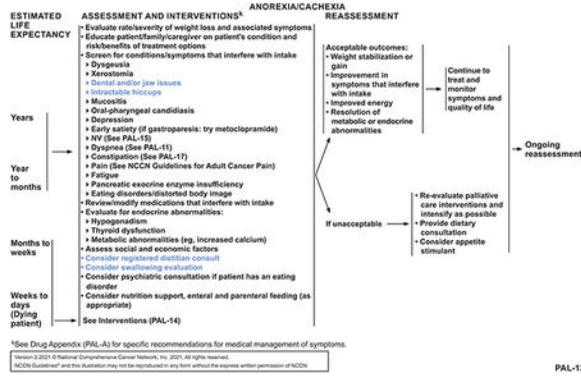
Primary palliative care, including both anticancer treatments and disease-related symptom management, should be provided for all patients. Anticancer therapy should be in line with standard practice as well as stated patient goals and priorities and be accompanied by appropriate prevention/management of adverse effects as well as palliation of physical and psychosocial symptoms. A longitudinal cohort study evaluated the impact of palliative chemotherapy on QoL near the end of life (median 3.8 months before death) as a function of patient performance status. For patients with progressive metastatic cancer in this study, palliative chemotherapy failed to improve QoL near death for those with moderate or poor performance status and worsened QoL near death for those with initially good performance status.<sup>24</sup> Additional studies have reported that anticancer therapy may continue beyond what is evidence-based for patients with advanced or metastatic disease.<sup>25-27</sup> This suggests a need for better prognostic awareness and iterative discussions of patient/family/caregiver values and goals of treatment.



### Symptom Management

Symptoms should be comprehensively assessed in all patients. In noncommunicative patients, symptom intensity may be assessed using physical signs. Education should be provided to the patient/family/caregiver on the patient’s condition and the risk/benefit of treatment options. At the most recent meeting to update the NCCN Guidelines, the panel added a recommendation that providing resources for the psychosocial and emotional support of not only the patient but also family/caregiver(s) be considered an integral part of symptom management. As a general principle, when appropriate, providers should try to use palliative interventions that may address multiple symptoms.

**Pain**—The patient and family/caregiver should be educated on the role of pain medications, customized to the patient’s particular situation. In addition, it is important to note that dying patients in their last weeks of life may have different needs than patients at earlier disease stages. For instance, if feasible or desired, pain management may need to be balanced against reduced level of consciousness. In advanced cancer, opioids may need to be titrated aggressively for moderate/severe acute/chronic pain.<sup>28</sup> Single-fraction palliative radiotherapy may also be used to address pain associated with bone metastases.<sup>29-32</sup> A recent systematic review also found that terminally ill patients receiving nonpharmacologic therapy in addition to medication experienced greater physical symptom relief and overall mood improvement.<sup>33</sup> The panel recommends consideration of nonpharmacologic and/or integrative interventions as an additional source of pain management. Examples include cognitive behavioral therapy and acceptance and commitment therapy; massage; art or music therapy; application of hot or cold packs; repositioning; and use of supportive braces.<sup>31-39</sup> For pain refractory to all of these interventions, palliative sedation may be considered following consultation with pain management or palliative care specialists, consistent with local institutional policies.



**Anorexia/Cachexia**—Cachexia is physical wasting with loss of skeletal and visceral muscle mass and is very common among patients with advanced cancer.<sup>40,41</sup> Many patients with cancer lose the desire to eat (anorexia), which contributes to cachexia. Cachexia can also occur independently from anorexia, as proinflammatory cytokines and tumor-derived factors directly lead to muscle proteolysis.<sup>40,41</sup> Cachexia leads to asthenia (weakness), hypoalbuminemia, emaciation, immune system impairment, metabolic dysfunction, and autonomic failure. Cancer-related cachexia has also been associated with failure of anticancer treatment, increased treatment toxicity, delayed treatment initiation, early treatment termination, shorter survival, and psychosocial distress.<sup>40-42</sup> A study that examined cancer cachexia in a cohort of 1,473 patients across all weight ranges showed that muscle depletion conveys a similarly poor prognosis as involuntary weight loss, regardless of body mass index.<sup>43</sup>

Initial steps include evaluating the rate and severity of weight loss and associated symptoms, educating the patient/family/caregiver on the patient’s condition, and discussing the risks/benefits of available treatment options. During assessment, the panel strongly recommends considering a formal swallowing evaluation for patients who report dysphagia or exhibit symptoms that suggest possible swallowing dysfunction. The panel also suggests that clinicians assess for conditions or symptoms that interfere with food intake, such as dysgeusia, xerostomia, dental/jaw issues, intractable hiccups, mucositis, oropharyngeal candidiasis, depression, early satiety, nausea and vomiting, and pain. A psychiatric evaluation may be considered if there is suspicion or a history of an eating disorder. Treatment may include management of symptoms or discontinuation of medications that interfere with food intake, as well as improving a bowel regimen to optimize gut motility.<sup>44-46</sup> Strengthening social supports, dietary counseling, and feeding assistance may also be offered as nonpharmacologic management of cachexia.<sup>47</sup>

If increased appetite is an important aspect of the patient’s QoL, appetite stimulants may be helpful (eg, megestrol acetate, dexamethasone, olanzapine).<sup>48-52</sup> Systematic reviews and meta-analyses of megestrol acetate demonstrate improved appetite and slight improvements in weight gain.<sup>47,49</sup> However, benefits of using megestrol acetate should be balanced with the potential increased risk for venous thromboembolic events, fluid retention, and death, particularly in older patients or those who are nonambulatory.<sup>53-55</sup> Combining megestrol



acetate therapy with dietary counseling and nutritional supplements may yield improved outcomes for patients with preserved functional status and cancer cachexia.<sup>47</sup>

PALLIATIVE CARE DRUG APPENDIX

Condition	Recommended Agents and Dosage by Estimated Life Expectancy and Symptom Etiology
Dyspnea (PAL-11)	Life Expectancy: Years: Year to Months; and Months to Weeks • General: Morphine, 2.5–10 mg PO q2h PRN or 1–3 mg IV q2h PRN for opioid naïve, increase dose by 25% for opioid tolerant • For acute progressive dyspnea, or for patients who are not opioid naïve, more aggressive titration may be required • Anxiety: Lorazepam, 0.25–1 mg PO q4h PRN for benzodiazepine naïve
Dyspnea (PAL-12)	Life Expectancy: Weeks to Days (dying patient) • General: Morphine, 2.5–10 mg PO q2h PRN or 1–3 mg IV q2h PRN if opioid naïve, increase dose by 25% for opioid tolerant • For acute progressive dyspnea, or for patients who are not opioid naïve, more aggressive titration may be required • Anxiety: Lorazepam, 0.25–1 mg PO q4h PRN if benzodiazepine naïve • Fluid overload: Furosemide
Secretions (PAL-12)	• Excessive secretions: Scopolamine, 0.4 mg SC q4h PRN/1.5 mg patches, 1–3 patches q72h OR atropine, 1% ophthalmic solution 1–2 drops SL q4h PRN OR glycopyrrolate, 0.2–0.4 mg IV or SC q4h PRN
Anorexia/ <sup>a</sup> Cachexia <sup>a</sup> (PAL-13)	Life Expectancy: Years: Year to Months • Depression/anorexia: Mirtazapine, 7.5–30 mg PO QHS • Gastroparesis (early satiety): Metoclopramide 5–10 mg PO QID 30 min before meals and at bedtime • Loss of appetite: Margetroline acetate, 200–400 mg/d PO OR olanzapine, 5 mg/d PO
Anorexia/ <sup>a</sup> Cachexia <sup>a</sup> (PAL-14)	Life Expectancy: Months to Weeks; Weeks to Days (dying patient) • Loss of appetite: Megestrol acetate, 400–800 mg/d PO OR olanzapine, 5 mg/d PO OR dexamethasone, 3–4 mg/d PO OR • Depression: Mirtazapine, 7.5–30 mg PO QHS

<sup>a</sup>Rosland EA, Buhix K, Baracos VE, et al. Management of Cancer Cachexia. ASCO Guideline. J Clin Oncol 2020;38(21):2438-2453.  
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PAL-A  
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### Summary

This article highlights recent updates to the 2021 version of the NCCN Guidelines for Palliative Care. Several recommendations were made by the panel to enhance the QoL of patient/family/caregivers throughout the disease trajectory. These include effectively assessing and addressing psychosocial distress, promoting adaptive coping strategies for patients/family/caregivers, and emphasizing the need for holistic cancer care plans that include patient/family/caregiver education and support. The panel acknowledged and recommended describing the palliative care team as “interprofessional” to emphasize its collaborative nature. Updates also included suggestions for a multimodal approach to the management of anorexia/cachexia.

### Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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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 noted.

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.

**PLEASE NOTE**

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are a statement of evidence and consensus of the authors regarding their views of currently accepted approaches to treatment. The NCCN Guidelines Insights highlight important changes in the NCCN Guidelines recommendations from previous versions. Colored markings in the algorithm show changes and the discussion aims to further the understanding of these changes by summarizing salient portions of the panel’s discussion, including the literature reviewed.

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