National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Palliative Care

Version 2.2012

NCCN.org

Continue

NCCN Guidelines Version 2.2012 Panel Members
Palliative Care

NCCN Guidelines Index
Palliative Care TOC
Discussion

* **Michael H. Levy, MD, PhD/Chair** † £
Fox Chase Cancer Center

Michael D. Adolph, MD, MPH, MBA, FACS
The Ohio State University Comprehensive Cancer Center - James Cancer Hospital and Solove Research Institute

Anthony Back, MD † £
Fred Hutchinson Cancer Research Center/Seattle Cancer Care Alliance

Susan Block, MD £ θ
Dana-Farber/Brigham and Women's Cancer Center

Shirley N. Codada, MD £ Þ
H. Lee Moffitt Cancer Center & Research Institute

Shalini Dalal, MD £
The University of Texas MD Anderson Cancer Center

Teresa L. Deshields, PhD θ
Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine

Elisabeth Dexter, MD
Roswell Park Cancer Institute

NCCN
Deborah Freedman-Cass, PhD
Mary Anne Bergman

Sydney M. Dy, MD £
The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

Sara J. Knight, PhD θ
UCSF Helen Diller Family Comprehensive Cancer Center

Sumathi Misra, MD Þ £ ₪
Vanderbilt-Ingram Cancer Center

Christine S. Ritchie, MD, MSPH ₪ £
University of Alabama at Birmingham Comprehensive Cancer Center

Todd M. Sauer, MD £
UNMC Eppley Cancer Center at The Nebraska Medical Center

Thomas Smith, MD
The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

David Spiegel, MD θ
Stanford Cancer Institute

Linda Sutton, MD † £
Duke Cancer Institute

Robert M. Taylor, MD £ Ψ
The Ohio State University Comprehensive Cancer Center - James Cancer Hospital and Solove Research Institute

Jennifer Temel, MD † £
Massachusetts General Hospital Cancer Center

Jay Thomas, MD, PhD Þ £
City of Hope Comprehensive Cancer Center

Roma Tickoo, MD, MPH
Memorial Sloan-Kettering Cancer Center

Susan G. Urba, MD † £
University of Michigan Comprehensive Cancer Center

Jamie H. Von Roenn, MD † £
Robert H. Lurie Comprehensive Cancer Center of Northwestern University

Joseph L. Weems, MD
St. Jude Children`s Research Hospital/ University of Tennessee Cancer Institute

Sharon M. Weinstein, MD, FAAHPM £ Ψ
Huntsman Cancer Institute at the University of Utah

‡ Hematology/hematology oncology
† Medical oncology
Þ Internal medicine
£ Supportive care including palliative and pain management
θ Psychiatry and psychology, including health behavior
Ψ Neurology/neuro-oncology
φ Anesthesiology
₪ Geriatric medicine
* Writing committee member

Continue

NCCN Guidelines Panel Disclosures

NCCN Guidelines Version 2.2012 Table of Contents Palliative Care

NCCN Guidelines Index
Palliative Care TOC
Discussion

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

To find clinical trials online at NCCN member institutions, click here: nccn.org/clinical_trials/physician.html

NCCN Categories of Evidence and Consensus: All recommendations are Category 2A unless otherwise specified.

See NCCN Categories of Evidence and Consensus

NCCN Guidelines Version 2.2012 Updates Palliative Care

NCCN Guidelines Index
Palliative Care TOC
Discussion

The 2.2012 version of the Palliative Care Guidelines represents the addition of the updated discussion section - MS-1.

Updates in Version 1.2012 of the Palliative Care Guidelines from Version 1.2011 include:

PAL-1

- Definition of Palliative Care:
  - The definition has been modified with footnote "a" new to the page.
- Standard of Palliative Care:
  - 1st bullet, "Institutions should develop processes for integrating palliative care into cancer care, both as part of usual oncology care and for patients with specific palliative care needs," is new to the page.
  - 5th bullet, "Skilled, palliative care specialists and interdisciplinary, palliative care teams," was modified by adding, "including board-certified palliative care physicians" should be readily available to provide consultative or direct care to patients/families who request or require their expertise."
  - Footnote "b" is new to the page.

PAL-2

- Not Present:
  - 1st sub-bullet under "Inform patients and families," "Discuss anticipation and prevention of symptoms" was modified by adding, "and advance care planning." (Also for PAL-3)
  - Footnote "c" was modified by including, "nurse practioners, physician assistants, and dietitians." (Also for PAL-3 and PAL-7).
  - Footnote "d": "Early consultation/collaboration with a palliative care specialist/hospice team" was modified by adding, "should be considered to" improve quality of life and survival."
    (Also for PAL-3 and PAL-7).
- Reassessment:
  - Changed "Satisfactory Outcome" to "Acceptable" and "Unsatisfactory Outcome" to "Unacceptable" (Throughout the guideline).

PAL-3

- Screening:
  - 3rd bullet, "serious comorbid physical and psychosocial conditions" was modified by including "psychiatric."
  - 4th bullet, "life expectancy ≤12 mo" was modified to "6 mo."
  - 4th bullet, 1st indented sub-bullet, "many stage IV cancers" is new to the page.
- Assessment: the title was modified by adding, "Oncology Team." (Also for PAL-4).

PAL-4

- Assessment by Oncology Team:
  - 3rd bullet, "potential for treatment-related toxicities" is new to the page.
- Psychosocial distress:
  - "Consider Consultation with Palliative Care Specialist" is new to the page.
  - 1st sub-bullet under "Social support problems," "Home" is new to the page.

PAL-6

- Criteria for Consultation with Palliative Care Specialists:
  - 3rd bullet, "Non-pain physical symptoms refractory to conventional management," was modified by adding,"high symptom burden."
  - 11th bullet, "Inability to engage in advanced care planning and care plan" is new to the page.

PAL-7

- "Intervention" was changed to "Oncology Team Interventions."
  - 2nd bullet was modified to include, collaborate with "other health care professionals."
- Unacceptable:
  - 1st bullet was modified to read, "Intensify "palliative care" efforts to communicate palliative care options."
  - 2nd bullet was modified to read, "Consult with a "mental health professional" to evaluate and treat "undiagnosed" psychiatric disorders, substance abuse, and "inadequate coping methods."

PAL-8

- Interventions, Years to months:
  - 5th bullet, "Prepare patient psychologically for possible disease progression" is new to the page.
- Interventions, Months to weeks:
  - 5th bullet, "Consider potential discontinuation of anticancer treatment" is new to the page.
- Interventions, Weeks to days:
  - 1st bullet, was modified by adding, "Encourage discontinuation of" anticancer therapy.

PAL-10

- Dyspnea:
  - 2nd sub-bullet under Interventions, "Therapeutic procedure for cardiac, pleural, or abdominal fluid" is new to the page.

NCCN Guidelines Version 2.2012 Updates Palliative Care

NCCN Guidelines Index
Palliative Care TOC
Discussion

Updates in Version 1.2012 of the Palliative Care Guidelines from Version 1.2011 include:

PAL-10 (continued)
- Relieve symptoms:
  - 2nd sub-bullet, "Educational, psychosocial, and emotional support" was modified to include, "for the patient and family."
  - 4th sub-bullet was modified to read, "If opioid naive, morphine, 2.5-10 mg PO q 4 hr prn, "1-3 mg IV q 1 hr prn."
  - Footnote "f": "For acute progressive dyspnea, more aggressive titration may be required" is new to the page. (Also for PAL-11).

PAL-11
- Relieve symptoms:
  - 1st sub-bullet, "Fans" is new to the page.
  - 2nd sub-bullet, "Oxygen if hypoxic and/or subjective relief is reported" is new to the page.
  - 6th sub-bullet, Reduce excessive secretions, "glycopyrrolate 0.2-0.4 mg IV or SQ q 4 hr prn" was added as another option to control secretions.
- Footnote "g" is new to the page.

PAL-12
- Interventions, Symptoms that interfere with intake:
  - 3rd sub-bullet, "Oral-pharyngeal candidiasis" is new to the page.
  - 7th sub-bullet, "Depression" was modified to include "Anorexia" and "Mirtazapine (7.5-30 mg hs)."
  - 3rd bullet now includes "prednisone 10-20 mg BID"
  - 7th bullet has been modified to include, "enteral and parenteral feeding, as appropriate."
  - Footnote "h" is new to the page.
  - Footnote "i" is new to the page.

PAL-13
- Anorexia/Cachexia Interventions:
  - 1st sub-bullet has been modified to read, "If important, consider short course of prednisone 10-20 mg BID."
  - 5th bullet, "Mirtazapine 7.5-30 mg hs" was added to treat depression.
  - 6th bullet, "Provide education and support to the patient and family regarding emotional aspects of withdrawal of nutritional support" is new to the page.
  - 7th sub-bullet has been modified to read, "Withholding or withdrawal of enteral or parenteral nutrition is ethically permissible in this setting. It will not cause exacerbation of symptoms and may improve some symptoms."

PAL-14
- Nausea and Vomiting Interventions:
  - 3rd bullet was modified to read, "Gastroparesis (metoclopramide, 5-20 mg po qid 30 min before meals and at bedtime)"

PAL-16
- Constipation, Interventions:
  - 3rd bullet, "consider GI consult" is new to the page.

PAL-17
- Weeks to days (Dying patient):
  - 3rd bullet, "Provide education and support to the patient and family" is new to the page.

PAL-18
- Pharmacologic management:
  - 5th sub-bullet, "Corticoteroids: dexamethasone 6-16 mg IV daily" is new to the page.
  - 6th bullet, "Nasogastric (NG)" has been modified to "Enteral."

PAL-19
- Interventions:
  - 1st bullet, "Explore fears and anxiety regarding death/disease" is new to the page.
  - 4th sub-bullet, "Restless leg syndrome" with "Ropinirole 0.25-4 mg PO at bedtime" is new to the page.
- Insomnia:
  - "Trazodone, 25-100 mg PO at bedtime," is new to the page.
  - "Mirtazapine, 7.5-30 mg PO at bedtime," is new to the page.
  - Footnote "p": "Effectiveness of mirtazapine for nausea and insomnia in cancer patients with depression" is new to the page.
- Daytime sedation:
  - "Caffeine 100-200 mg PO q 6 hrs, last dose at 4 PM" is new to the page.
  - "Methylphenidate" has been modified to read, "start with 2.5-5 mg PO BID – 20 mg BID second dose no later than noon."
  - "Dextroamphetamine, 2.5 mg up to 5-10 mg BID, no later than noon" is new to the page.
  - "Modafinil" has been modified to read, "100-400 mg PO each morning."

NCCN Guidelines Version 2.2012 Updates Palliative Care

NCCN Guidelines Index
Palliative Care TOC
Discussion

Updates in Version 1.2012 of the Palliative Care Guidelines from Version 1.2011 include:

PAL-19 (continued)
- Adjust doses of pharmacologic therapies:
  - "Consider chlorpromazine," has been modified to read, "25-100 mg PO/PR at bedtime."
  - "Consider quetiapine 25-50 mg PO at bedtime" is new to the page.

PAL-20
- Delirium Interventions:
  - 1st bullet, "Avoid benzodiazepines unless patient has refractory delirium on antipsychotics" is new to the page.
  - 3rd bullet, "olanzapine" has been modified to read, "2.5-7.5 mg/d PO/IV q 2-4 h prn (maximum = 30 mg/d)."
  - "Chlorpromazine" has been modified to read "25-100 mg PO/PR/IV q 4 h prn for bed bound patients."
  - "Lorazepam" has been modified to read, "0.5-2 mg SQ/IV q 4 h."
  - 6th bullet, "Consider opioid dose reduction or rotation" is new to the page.

PAL-21
- Delirium, Interventions:
  - 7th bullet, "failure" was changed to "function."

PAL-22
- Social Support/Resource Management, Interventions:
  - 9th bullet was modified to read, "Discuss personal, spiritual, and cultural issues relating to illness and prognosis."
  - 10th bullet was modified to read, "Obtain medical interpreters/translators who are not related to the patient and family as needed." (Also for PAL-23)

PAL-23
- Social Support/Resource Management Intervention:
  - 8th bullet was modified to read, "Consider palliative care consultation to assist in conflict resolution when patient, family, and/or professional team do not agree on benefit/utility of interventions."
- Reassessment/Unacceptable:
  - 3rd bullet was modified to read, "Consult or refer to specialized palliative care services, hospice, or ethics committee."

PAL-26
- Advance Care Planning, Interventions/Years/Years to months:
  - 4th bullet, "Initiate discussion of personal values and preferences for end-of-life care" is new to the page.
  - 5th bullet, "If patient values and goals lead to a clear recommendation regarding future treatment in light of disease status, physician should make a recommendation about future care" is new to the page.
  - 6th bullet, "Document patient values and preferences and any decisions in accessible site in medical record (including MOLST/POLST if completed)" is new to the page
- Advance Care Planning, Reassessment/Unacceptable:
  - 1st bullet, "Explore patient reluctance to engage in advance care planning" is new to the page. (Also for PAL-27)
  - 2nd bullet, "Explore fears and worries about illness" is new to the page. (Also for PAL-27)
  - 3rd bullet, "Refer to palliative care if the patient is having difficulty engaging in discussion of advance care planning" is new to the page. (Also for PAL-27)
  - 4th bullet, "Consider referral to a mental health clinician to evaluate mental health issues" is new to the page. (Also for PAL-27)

PAL-27
- Advance Care Planning, Interventions/Months to weeks:
  - 1st bullet, "Address months to years interventions" is new to the page.
  - 3rd bullet, "Confirm patient's values and decisions in light of changes in status" is new to the page.
  - 4th bullet, "If not previously done, make recommendation about appropriate medical treatment to meet patient's values and goals" is new to the page.
  - 5th bullet, "Ensure complete documentation of advance care plan in medical record, including MOLST/POLST if applicable, to assure accessability of plan to all providers across care settings" is new to the page.
  - 6th bullet, "Explore family concerns about patient's plan and seek resolution of conflict between patient and family goals and wishes" is new to the page.
  - 7th bullet, "Consider consultation with palliative care specialist to assist in conflict resolution when patient, family, and health care team disagree" is new to the page.

NCCN Guidelines Version 2.2012 Updates Palliative Care

NCCN Guidelines Index
Palliative Care TOC
Discussion

Updates in Version 1.2012 of the Palliative Care Guidelines from Version 1.2011 include:

PAL-27 (continued)
- Weeks to days (Dying patient):
  - 1st bullet, "Assure that all items identified above are complete" is new to the page.
  - 2nd bullet, "Implement and ensure compliance with advance care plan" is new to the page.
  - 3rd bullet, "Clarify and confirm patient's decision about life-sustaining treatments, including CPR, if necessary" is new to the page.
  - 4th bullet, "Explore desire for organ donation and/or autopsy" is new to the page.

PAL-28
- Response to Requests for Hastened Death:
  - 1st sentence of the 1st bullet has been modified to read, "The NCCN Palliative Care Panel believes that the most appropriate response to a request for assistance in suicide is to intensify palliative care. All such patients should be referred to a palliative care specialist."
  - 4th bullet, 5th sub-bullet has been modified to read, "Assess for fears of caregiver burden and abandonment and re-emphasize physician commitment to the patient."
  - 7th bullet, "Discuss alternatives to physician-assisted suicide such as withdrawal of life-sustaining treatment, voluntary cessation of eating or drinking, and/or sedation for refractory symptoms."
  - 9th bullet, 3rd sentence has been modified to read, "Physician-assisted suicide is legal only in Oregon, Montana, and Washington and has specific guidelines.

PAL-29
- Title modified to read, "Care of the Imminently Dying Patient"
- Physical:
  - 6th sub-bullet has been modified to include, "Adjust doses of medications to optimal comfort."
  - 8th sub-bullet is new to the page, "Treat dyspnea by adjusting the dose of medication (See PAL-10)."
- Practical:
  - 3rd sub-bullet has been modified to read, "Recommend that patient's wishes for resuscitation and/or do-not-resusciate (DNR) are documented and followed."
  - 1st sub-sub-bullet has been modified to read, "If patient/family have not documented a DNR order, intensify patient/family education and counsel family on importance of a DNR."

PAL-30
- Palliative Sedation:
  - 4th bullet, "Pentobarbitol: Initial infusion 2-3 mg per kg load then 1-2 mg per kg/h is new to the page.

PAL-31
- After-Death Interventions, Assessment:
  - A "good death" has been modified to read, a "peaceful death."
- After-Death Interventions/Immediate after-death care:
  - 2nd sub-bullet has been modified to read, "Remove tubes, drains, lines, and the foley catheter unless an autopsy is planned."
  - 3rd sub-bullet is new to the page, "Inform family (if not present) of death."
  - 7th sub-bullet has been modified to include "Offer condolences."
  - 4th bullet has been modified to read, "Identify family members at risk for complicated bereavement or prolonged grief disorder."
  - 11th bullet has been modified to read, "Identify health care professionals at risk of complicated bereavement, or moral distress, compassion fatigue."

DEFINITION OF PALLIATIVE CARE[a]

Palliative care is a special kind of patient and family-centered health care that focuses upon effective management of pain and other distressing symptoms, while incorporating psychosocial and spiritual care according to patient/family needs, values, beliefs, and cultures. The goal of palliative care is to anticipate, prevent, and reduce suffering and to support the best possible quality of life for patients and their families, regardless of the stage of the disease or the need for other therapies. Palliative care begins at diagnosis and should be delivered concurrently with disease-directed, life-prolonging therapies and should 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 initiated by the primary oncology team and then augmented by collaboration with an interdisciplinary team of palliative care experts.

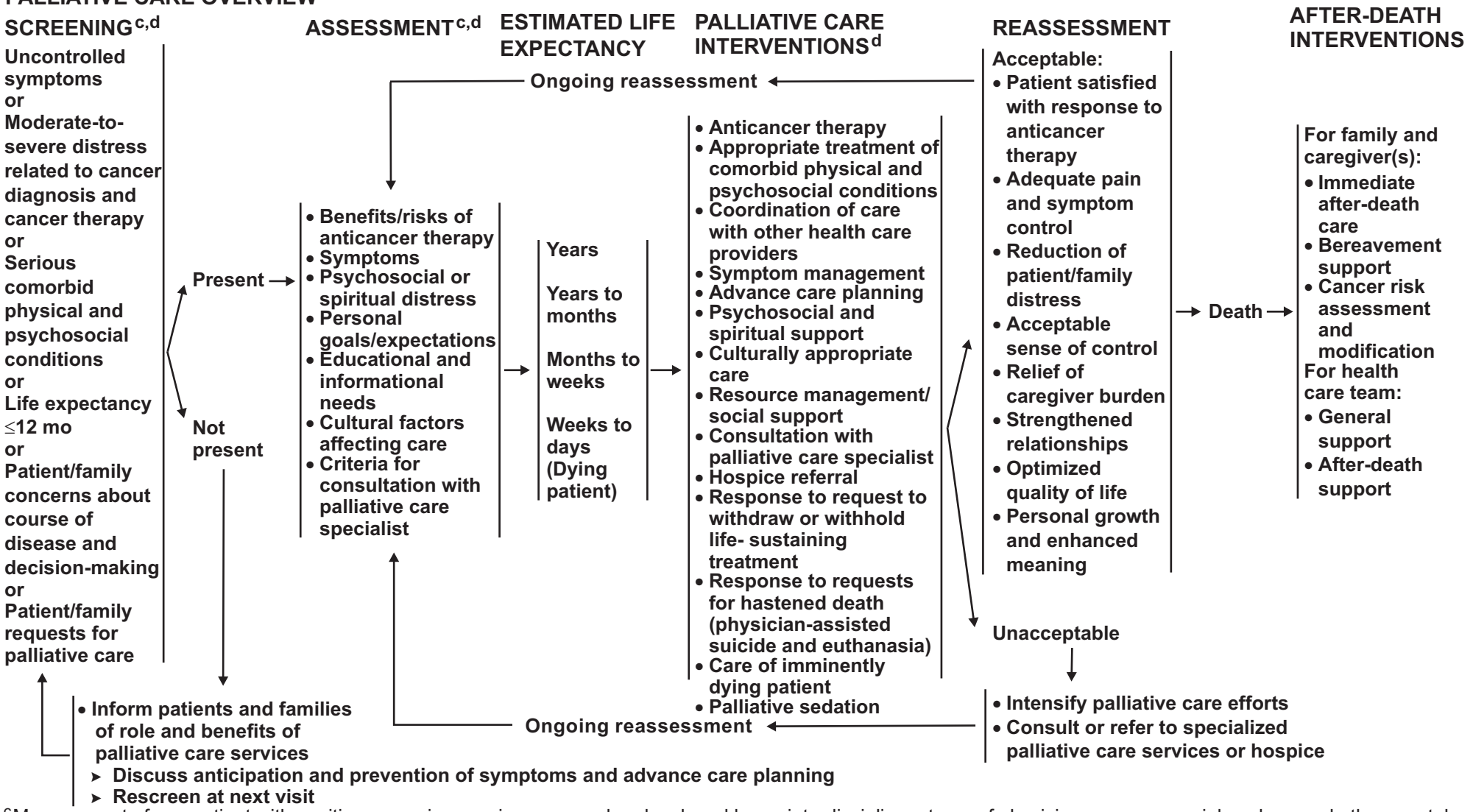
STANDARDS OF PALLIATIVE CARE[b]

- **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 and families 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.**
- **Skilled, palliative care specialists and interdisciplinary, palliative care teams, including board-certified palliative care physicians, advanced practice nurses and physician assistants should be readily available to provide consultative or direct care to patients/families who request or require their expertise.**
- **Quality of palliative care should be monitored by institutional quality improvement programs.**

[a] Hui D, Mori M, Parsons HA, et al. The lack of standard definitions in supportive and palliative oncology literature. J Pain Symptom Manage 2012;43:582-592.
[b] Ferris FD, Bruera E, Cherny N, et al. Palliative cancer care a decade later: accomplishments, the need, next steps – from the American Society of Clinical Oncology. J Clin Oncol 2009;27:3052-3058.

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

PALLIATIVE CARE OVERVIEW



[c]Management of any patient with positive screening requires a care plan developed by an interdisciplinary team of physicians, nurses, social workers and other mental health professionals, chaplains, nurse practitioners, physician assistants, and dietitians.

[d]Oncologists should integrate palliative care into general oncology care. Early consultation/collaboration with a palliative care specialist/hospice team should be considered to improve quality of life and survival.

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

Assessment by Oncology Team (PAL-3)

SCREENING[c,d]

- **Uncontrolled symptoms**
  or
- **Moderate-to-severe distress related to cancer diagnosis and/or cancer therapy**
  or
- **Serious comorbid physical, psychiatric, and psychosocial conditions**
  or
- **Life expectancy ≤6 mo**
  - **Indicators include:**
    - **Many stage IV cancers**
    - **Poor performance status**
      ECOG ≥3 or KPS ≤50
    - **Hypercalcemia**
    - **Brain or cerebrospinal fluid metastasis**
    - **Delirium**
    - **Superior vena cava syndrome**
    - **Spinal cord compression**
    - **Cachexia**
    - **Malignant effusions**
    - **Bilirubin ≥2.5 mg/dL**
    - **Creatinine ≥3 mg/dL**

  or
- **Patient/family concerns about course of disease and decision-making**
  or
- **Patient/family requests for palliative care**

ASSESSMENT BY ONCOLOGY TEAM

Present

- **Benefits/risks of anticancer therapy**
- **Symptoms**
- **Psychosocial distress**

→ **See PAL-4**

- **Personal goals/expectations**
- **Educational and informational needs**
- **Cultural factors affecting care**

→ **See PAL-5**

- **Criteria for consultation with a palliative care specialist**

→ **See PAL-6**

Not present

- **Inform the patient and family of the role and benefits of palliative care services**
  - **Discuss anticipation and prevention of symptoms and advance care planning**

Rescreen at next visit

[c]Management of any patient with positive screening requires a care plan developed by an interdisciplinary team of physicians, nurses, social workers and other mental health professionals, chaplains, nurse practitioners, physician assistants, and dietitians.

[d]Oncologists should integrate palliative care into general oncology care. Early consultation/collaboration with a palliative care specialist/hospice team should be considered to improve quality of life and survival.

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

ASSESSMENT BY ONCOLOGY TEAM

Benefits/risks of anticancer therapy →
- Natural history of specific tumor
- Potential for response to further treatment
- Potential for treatment-related toxicities
- Meaning of anticancer therapy to patient and family
- Impairment of vital organs
- Performance status
- Serious comorbid conditions

→ Anticancer therapy interventions (See PAL-8)

Symptoms →
- Pain → Pain Interventions (See PAL-9)
- Dyspnea → Dyspnea Interventions (See PAL-10)
- Anorexia/cachexia → Anorexia/Cachexia Interventions (See PAL-12)
- Nausea/vomiting (NV) → Nausea/Vomiting Interventions (See PAL-14)
- Constipation → Constipation Interventions (See PAL-16)
- Malignant bowel obstruction → Malignant Bowel Obstruction (See PAL-17)
- Fatigue/weakness/asthenia → See NCCN Cancer-Related Fatigue Guidelines
- Insomnia/sedation → Insomnia/Sedation Interventions (See PAL-19)
- Delirium → Delirium Interventions (See PAL-20)

Psychosocial distress →
- Psychosocial/psychiatric
  - Depression/anxiety
  - Illness-related distress
- Spiritual or existential crisis

→ See NCCN Distress Management Guidelines
→ Consider Consultation with Palliative Care Specialist (See PAL-6)

- Social support problems
  - Home
  - Family
  - Community
- Resources problems
  - Financial

→ Social Support/Resource Management (See PAL-22)

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

PALLIATIVE CARE ASSESSMENT

Personal goals/ expectations →

- Patient goals and expectations
  - ▸ Advance care planning
- Family goals and expectations
- Priorities for palliative care
  - ▸ Goals and meaning of anticancer therapy
  - ▸ Quality of life
- Eligibility for hospice, with needs that might be met by hospice

→ Interventions (See PAL-24)
Advance Care Planning (See PAL-26)

- Educational and informational needs
- Cultural factors affecting care

→

- Patient/family values and preferences about information and communication
- Patient/family perceptions of disease status

→ Interventions (See PAL-24)

Criteria for consultation with palliative care specialist → (See PAL-6)

Palliative Care Table of Contents

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

CRITERIA FOR CONSULTATION WITH PALLIATIVE CARE SPECIALIST

ASSESSMENT

Patient characteristics →

- Limited treatment options
- High risk of poor pain control or pain that remains resistant to conventional interventions, eg:
  - Neuropathic pain
  - Incident or breakthrough pain
  - Associated psychosocial and family distress
  - Rapid escalation of opioid dose
  - History of drug or alcohol abuse
  - Impaired cognitive function
- Non-pain physical symptoms refractory to conventional management, high symptom burden (See PAL-4 for symptoms)
- Multiple "allergies" or a history of multiple adverse reactions to pain and symptom management interventions
- Complicated ICU admissions (especially those with multiple complications or those requiring lengthy ventilator support)
- High distress score (>4) (See NCCN Distress Management Guidelines)
- Cognitive impairment
- Severe comorbid conditions
- Communication barriers[e]
- Requests for hastened death
- Inability to engage in advance care planning and care plan

Social circumstances or Anticipatory bereavement issues →

- Family/caregiver limitations
- Inadequate social support
- Intensely dependent relationship(s)
- Financial limitations
- Limited access to care
- Family discord
- Patient's concerns regarding care of dependents
- Spiritual or existential crisis
- Unresolved or multiple prior losses

→ See Oncology Team Interventions (PAL-7)

[e]Communication barriers include language, literacy, and physical barriers.

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

ONCOLOGY TEAM INTERVENTIONS

- Consult with palliative care specialist/team[c,d]
- Collaborate with other health care professionals treating the patient
- Refer to appropriate health care professionals
  - Mental health and social services
  - Health care interpreters
  - Others
- Mobilize community support
  - Religious
  - School
  - Community agencies
- Expedite referral to hospice services when appropriate

REASSESSMENT

Acceptable:
- Patient satisfied with response to anticancer therapy
- Adequate pain and symptom control
- Reduction of patient/family distress
- Acceptable sense of control
- Relief of caregiver burden
- Strengthened relationships
- Optimized quality of life
- Personal growth and enhanced meaning
- Advance care planning in progress

→ Ongoing reevaluation and communication between the patient and health care team

Unacceptable →
- Intensify palliative care efforts to communicate palliative care options
- Consult with a mental health professional to evaluate and treat undiagnosed psychiatric disorders, substance abuse, and inadequate coping methods
- See NCCN Distress Management Guidelines

→ Ongoing reassessment

[c]Management of any patient with positive screening requires a care plan developed by an interdisciplinary team of physicians, nurses, social workers and other mental health professionals,chaplains, nurse practitioners, physician assistants, and dietitians.

[d]Oncologists should integrate palliative care into general oncology care. Early consultation/collaboration with a palliative care specialist/hospice team should be considered to improve quality of life and survival.

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

BENEFITS/RISKS OF ANTICANCER THERAPY

ESTIMATED LIFE EXPECTANCY	INTERVENTIONS	REASSESSMENT		
Years Years to months →	• Discuss intent, goals, benefits, and risks of anticancer therapy, including possible effects on quality of life • Provide appropriate anticancer therapy as outlined in NCCN disease-specific guidelines • Provide appropriate prevention and management of symptoms caused by anticancer therapy • Provide appropriate palliative care • Prepare patient psychologically for possible disease progression	Acceptable: • Adequate pain and symptom control • Reduction of patient/family distress • Acceptable sense of control • Relief of caregiver burden • Strengthened relationships • Optimized quality of life • Personal growth and enhanced meaning →	Continue anticancer therapy and palliative care	
Months to weeks →	• See above interventions • Offer best supportive care, including referral to palliative care or hospice • Redirect goals and hopes to those that are achievable • Provide guidance regarding anticipated course of disease • Consider potential discontinuation of anticancer treatment			
Weeks to days (Dying patient) →	• Encourage discontinuation of anticancer therapy • Intensify palliative care in preparation for death • Provide guidance regarding anticipated dying process • Focus on symptom control and comfort • Foster patient participation in preparing loved ones • Refer to palliative care/hospice team	Unacceptable →	• Change or discontinue anticancer therapy • Review patient hopes about and meaning of anticancer therapy • Intensify palliative care efforts • Review advance care planning • Consult or refer to specialized palliative care services or hospice	Ongoing reassessment

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

PAIN

ESTIMATED LIFE EXPECTANCY	INTERVENTIONS	REASSESSMENT
Years Years to months Months to weeks	→ Treat according to NCCN Adult Cancer Pain Guidelines	
Weeks to days (Dying patient)	• Treat according to NCCN Adult Cancer Pain Guidelines In addition: • Do not reduce dose of opioid solely for decreased blood pressure, respiration rate, or level of consciousness • Maintain analgesic therapy; titrate to optimal comfort • Recognize and treat opioid-induced neurotoxicity, including myoclonus and hyperalgesia • If opioid reduction is indicated, reduce by ≤50% per 24 h to avoid acute opioid withdrawal or pain crisis. Do not administer opioid antagonist • Balance analgesia against reduced level of consciousness based on patient preference • Modify routes of administration as needed (PO, IV, PR, subcutaneous, sublingual, transmucosal, and transdermal) applying equianalgesic dose conversions • Consult with a pain management/palliative care specialist ▸ Consider sedation for refractory pain (See PAL-30)	Acceptable: • Adequate pain and symptom control • Reduction of patient/family distress • Acceptable sense of control • Relief of caregiver burden • Strengthened relationships • Optimized quality of life • Personal growth and enhanced meaning → • Continue to treat according to NCCN Adult Cancer Pain Guidelines • Monitor symptoms and quality of life to determine whether additional end-of-life measures are required → Ongoing reassessment Unacceptable → • Continue to treat according to NCCN Adult Cancer Pain Guidelines • Consider a consultation with a pain management/ palliative care specialist → Ongoing reassessment

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

DYSPNEA

ESTIMATED LIFE EXPECTANCY

INTERVENTIONS

- Assess symptom intensity
- Treat underlying causes/comorbid conditions:
  - Radiation/chemotherapy
  - Therapeutic procedure for cardiac, pleural, or abdominal fluid
  - Bronchoscopic therapy
  - Bronchodilators, diuretics, steroids, antibiotics, or transfusions
- Relieve symptoms
  - Oxygen therapy for hypoxia
  - Educational, psychosocial, and emotional support for the patient and family
  - Nonpharmacologic therapies, including fans, cooler temperatures, stress management, relaxation therapy, and physical comfort measures
  - If opioid naive, morphine, 2.5-10 mg PO q 4 hr prn, 1-3 mg IV q 1 hr prn[f]
  - Benzodiazepines (if benzodiazepine naive, starting dose lorazepam, 0.5-1 mg PO q 4 hr prn)
  - Temporary ventilatory (CPAP, BiPAP) support if clinically indicated for severe reversible condition

REASSESSMENT

Years

Years to months →

Months to weeks

Acceptable:
- Adequate dyspnea and symptom control
- Reduction of patient/family distress
- Acceptable sense of control
- Relief of caregiver burden
- Strengthened relationships
- Optimized quality of life
- Personal growth and enhanced meaning

→ Continue to treat and monitor symptoms and quality of life to determine whether status warrants change in strategies → **Ongoing reassessment**

Unacceptable →
- Intensify palliative care efforts
- Consult or refer to specialized palliative care services or hospice

Weeks to days (Dying patient) → See Interventions (PAL-11)

[f]For acute progressive dyspnea, more aggressive titration may be required.

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

DYSPNEA

ESTIMATED LIFE EXPECTANCY

- Years
- Years to months → See Interventions (PAL-10)
- Months to weeks → See Interventions (PAL-10)
- Weeks to days (Dying patient) →

INTERVENTIONS

- Assess symptom intensity
  - Use physical signs of distress as potential dyspnea in noncommunicative patients
- Focus on comfort
  - Continue to treat underlying condition as appropriate
- Relieve symptoms
  - Fans
  - Oxygen if hypoxic and/or subjective relief is reported
  - Nonpharmacologic therapies; educational, psychosocial, and emotional support (See PAL-10)
  - If opioid naive, morphine, 2.5-10 mg PO q 4 hr prn, 1-3 mg IV q 1 hr prn[f]
  - Benzodiazepines (if benzodiazepine naive, starting dose lorazepam, 0.5-1 mg PO q 1 hr prn)
  - Reduce excessive secretions[g] with scopolamine, 0.4 mg SC q 4 hr prn; 1.5 mg patches, 1-6 patches q 3 d; atropine 1% ophthalmic solution 1-2 drops SL q 4 h pr; or glycopyrrolate 0.2-0.4 mg IV or SQ q 4 hr prn
- Withhold/withdraw/initiate time-limited trial of mechanical ventilation as indicated
  - Address patient and family preferences, prognosis, and reversibility
  - Provide sedation as needed
- Discontinue fluid support/consider low-dose diuretics if fluid overload may be a contributing factor
- Provide anticipatory guidance for patient/family regarding dying of respiratory failure
- Provide emotional and spiritual support

REASSESSMENT

Acceptable:

- Adequate dyspnea and symptom control
- Reduction of patient/family distress
- Acceptable sense of control
- Relief of caregiver burden
- Strengthened relationships
- Optimized quality of life
- Personal growth and enhanced meaning

→ Continue to treat and monitor symptoms and quality of life to determine whether status warrants change in strategies → Ongoing reassessment

Unacceptable →

- Intensify palliative care interventions and consider a consultation with a palliative care specialist
- Consider sedation for intractable symptoms (See PAL-30)

[f]For acute progressive dyspnea, more aggressive titration may be required.

[g]Hughes A et al. Audit of three antimuscarinic drugs for managing retained secretions. Palliative Medicine. 2000; 14:221-222.

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

ANOREXIA/CACHEXIA

ESTIMATED LIFE EXPECTANCY

INTERVENTIONS

- Evaluate rate/severity of weight loss
- Treat readily reversible cause of anorexia:
  - ➤ Early satiety
    - ◊ Metoclopramide
  - ➤ Symptoms that interfere with intake
    - ◊ Dysgeusia
    - ◊ Xerostomia
    - ◊ Oral-pharyngeal candidiasis
    - ◊ Mucositis
    - ◊ Nausea and/or Vomiting
    - ◊ Dyspnea
    - ◊ Depression/Anorexia (Mirtazapine 7.5-30 mg hs)
    - ◊ Constipation
    - ◊ Pain
    - ◊ Fatigue
    - ◊ Eating disorders/body image
- Review/modify medications that interfere with intake
- Evaluate for endocrine abnormalities:
  - ➤ Hypogonadism
  - ➤ Thyroid dysfunction
  - ➤ Metabolic abnormalities (eg, increased calcium)
- Consider appetite stimulant (eg, megestrol acetate, 400-800 mg/d; prednisone 10-20 mg BID)[h]
- Consider an exercise program
- Assess social and economic factors
- Consider nutrition consult
- Consider nutrition support, enteral and parenteral feeding[i] (as appropriate)

Years → Years to months

Months to weeks

Weeks to days (Dying patient) → See Interventions (PAL-13)

REASSESSMENT

Acceptable:

- Weight stabilization or gain
- Improvement in symptoms that interfere with intake
- Improved energy
- Resolution of metabolic or endocrine abnormalities

→ Continue to treat and monitor symptoms and quality of life to determine whether status warrants change in strategies → Ongoing reassessment

Unacceptable →

- Intensify palliative care interventions
- Provide dietary consultation
- Consider clinical trial

[h] Dy S, Lorenz K, et al. Evidence-Based Recommendations for Cancer Fatigue, Anorexia, Depression, and Dyspnea. 2008 J Clin Oncol. 26:3886-3895.

[i] August DA, Huhmann MB. A.S.P.E.N. clinical guidelines: nutrition support therapy during adult anticancer treatment and in hematopoietic cell transplantation. American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) JPEN J Parenter Enteral Nutr. 2009 Sep-Oct;33(5):472-500.

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

ANOREXIA/CACHEXIA

ESTIMATED LIFE EXPECTANCY

Years →

Years to months

Months to weeks

Weeks to days (Dying patient) →

INTERVENTIONS

See Interventions (PAL-12)

- Assess importance of symptoms of anorexia and cachexia to patient and family
  - If important, consider short course of prednisone 10-20 mg BID
- Focus on patient goals and preferences
- Provide family with alternate ways of caring for the patient
- Provide emotional support
- Treat for depression, if appropriate (Mirtazapine 7.5-30 mg hs)
- Provide education and support to patient and family regarding emotional aspects of withdrawal of nutritional support.
- Inform patient and family of natural history of disease, including the following points:
  - Absence of hunger and thirst is normal in the dying patient
  - Nutritional support may not be metabolized in patients with advanced cancer
  - There are risks associated with artificial nutrition and hydration, including fluid overload, infection, and hastened death
  - IV hydration may increase excretion of drug metabolites providing benefit to the patient
  - Symptoms like dry mouth should be treated with local measures, eg, mouthcare, small amounts of liquids
  - Withholding or withdrawal of enteral or parenteral nutrition is ethically permissible in this setting. It will not cause exacerbation of symptoms and may improve some symptoms

REASSESSMENT

Ongoing reassessment

Acceptable:
- Adequate anorexia/cachexia symptom control
- Reduction of patient/family distress
- Acceptable sense of control
- Relief of caregiver burden
- Strengthened relationships
- Optimized quality of life
- Personal growth and enhanced meaning

→ **Continue to treat and monitor symptoms and quality of life to determine whether status warrants change in strategies**

Unacceptable →
- Intensify palliative care efforts
- Consult or refer to specialized palliative care services or hospice

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

NAUSEA AND VOMITING

ESTIMATED LIFE EXPECTANCY

INTERVENTIONS[k,l]

Years

Years to months

Months to weeks[j]

Weeks to days (Dying patient)[j]

- **Chemotherapy/radiation therapy-induced**
  See NCCN Antiemesis Guidelines
- **Severe constipation/fecal impaction.**
  (See PAL-16)
- **Gastroparesis (metoclopramide, 5-20 mg po qid 30 min before meals and at bedtime)**
- **Bowel obstruction (See PAL-17)**
- **Central nervous system (CNS) involvement (eg, brain, meninges)**
  - **Corticosteroids (dexamethasone, 4-8 mg tid-qid)**
  - **Palliative radiation therapy**
- **Gastric outlet obstruction (squashed stomach syndrome) from intra-abdominal tumor and liver metastasis**
  - **If not contraindicated by comorbid conditions, treat with corticosteroids, proton pump inhibitor, metoclopramide, and consider stenting**
- **Metabolic abnormalities**
  - **Correct hypercalcemia**
  - **Treat dehydration**
- **Medication-induced**
  - **Discontinue any unnecessary medications**
  - **Check available blood levels of necessary medications (eg, digoxin, phenytoin, carbamazepine, tricyclic antidepressants)**
  - **Treat medication-induced gastropathy (eg, proton pump inhibitor, metoclopramide)**
  - **If due to opioids, initiate opioid rotation and/or consider reducing opioid requirement with non-nauseating coanalgesics or anesthesiologic/neurosurgical procedures**
- **Psychogenic**
  - **Consider psychiatric consultation if patient has an eating disorder, somatization, phobia, or panic disorder causing NV**
- **Non-specific NV**
  - **Initiate pharmacologic management with dopamine receptor antagonists (eg, haloperidol, metoclopramide, prochlorperazine)**
  - **If anxiety contributes to NV, consider adding lorazepam, 0.5-1 mg q 4 hr prn**
  - **If oral route is not feasible, consider rectal, subcutaneous, or intravenous administration of antinausea therapy**

If NV stops:
See Reassessment (PAL-15)

If NV persists:
See Interventions (PAL-15)

[j] In patients with advanced cancer, NV may be secondary to the cachexia syndrome (chronic nausea, anorexia, asthenia, changing body image, and autonomic failure).
[k] An around-the-clock dosing schedule would likely provide the greatest benefit to the patient.
[l] Continuous intravenous or subcutaneous infusions of different antiemetics may be necessary for the management of intractable NV.

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

PERSISTENT NAUSEA AND VOMITING

INTERVENTIONS

Titrate dopamine receptor antagonist (eg, prochlorperazine, haloperidol, metoclopramide) to maximum benefit and tolerance

↓

Add a 5-HT3 antagonist (eg, ondansetron) ± anticholinergic agent (eg, scopolamine) ± antihistamine (eg, meclizine) ± cannabinoid.
If NV persists:

↓

Add a corticosteroid (eg, dexamethasone).
If NV persists:

↓

Consider using a continuous IV/SC infusion of antiemetics; consider an opioid rotation if patient is on opioids.
If NV persists:

↓

Consider adding alternative therapies (eg, acupuncture, hypnosis, cognitive behavioral therapy)

REASSESSMENT

Acceptable:
- Adequate NV symptom control
- Reduction of patient/family distress
- Acceptable sense of control
- Relief of caregiver burden
- Strengthened relationships
- Optimized quality of life

→ Continue to treat and monitor symptoms and quality of life to determine whether status warrants change in strategies

→ Ongoing reassessment
See Interventions (PAL-14)

Unacceptable →
- Intensify palliative care efforts
- Consult or refer to specialized palliative care services or hospice
- Consider palliative sedation (See PAL-30)

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

CONSTIPATION

ESTIMATED LIFE EXPECTANCY

- Years
- Years to months
- Months to weeks
- Weeks to days (Dying patient)

INTERVENTIONS

Preventive measures

- Increase fluids
- Increase dietary fiber if patient has adequate fluid intake and physical activity
- Exercise, if appropriate
- Administer prophylactic medications
  - Stimulant laxative ± stool softener (senna ± docusate, 2 tablets every night)
  - Increase dose of laxative ± stool softener (senna ± docusate, 2-3 tablets bid-tid) with goal of 1 non-forced bowel movement every 1-2 days

If constipation is present:

- Assess for cause and severity of constipation
- Rule out impaction, especially if diarrhea accompanies constipation (overflow around impaction)
- Rule out obstruction (physical exam, abdominal x-ray/consider GI consult)
- Treat other causes (eg, hypercalcemia, hypokalemia, hypothyroidism, diabetes mellitus, medications)
- Add and titrate bisacodyl 10-15 mg daily-tid with a goal of 1 non-forced bowel movement every 1-2 days
- If impacted:
  - Administer glycerine suppository ± mineral oil retention enema
  - Perform manual disimpaction following pre-medication with analgesic ± anxiolytic

If constipation persists:

- Reassess for cause and severity of constipation
- Recheck for impaction or obstruction
- Consider adding other laxatives, such as bisacodyl (one suppository rectally daily-bid); polyethelene glycol (1 capful/8 oz water bid); lactulose, 30-60 mL bid-qid; sorbitol, 30 mL every 2 h x 3, then prn; magnesium hydroxide, 30-60 mL daily-bid; or magnesium citrate, 8 oz daily
- Consider methylnaltrexone for opioid- induced constipation, 0.15 mg/kg SC every other day, no more than once a day
- Tap water enema until clear
- Consider use of a prokinetic agent (eg, metoclopramide, 10-20 mg PO qid)

REASSESSMENT

Acceptable:

- Adequate constipation symptom control
- Reduction of patient/family distress
- Acceptable sense of control
- Relief of caregiver burden
- Strengthened relationships
- Optimized quality of life

→ Continue to treat and monitor symptoms and quality of life to determine whether status warrants change in strategies

→ Ongoing reassessment

Unacceptable →

- Intensify palliative care efforts
- Consult or refer to specialized palliative care services or hospice

→ Ongoing reassessment

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

MALIGNANT BOWEL OBSTRUCTION[m]

ESTIMATED LIFE EXPECTANCY	ASSESSMENT		
Years Years to months	• Screen for and treat underlying benign reversible causes ▸ Adhesions ▸ Radiation-induced strictures ▸ Internal hernias • Assess for malignant causes ▸ Tumor mass ▸ Carcinomatosis • Assess the goals of treatment for the patient, which can help guide the intervention[n] (eg, decrease NV, allow patient to eat, decrease pain, allow patient to go home/to hospice)	→	See Interventions (PAL-18)
Months to weeks Weeks to days (Dying patient)[n]	• Consider medical management rather than surgical management • Assess the goals of treatment for the patient, which can help guide the intervention[n] (eg, decrease NV, allow patient to eat, decrease pain, allow patient to go home/to hospice) • Provide education and support to patient and family	→	• Pharmacologic management • Intravenous or subcutaneous fluids • Enteral tube drainage ▸ Consider only if other measures fail to reduce vomiting • Endoscopic management → See Reassessment (PAL-18)

[m] Plain film radiography evaluation is usually enough to establish the diagnosis of bowel obstruction. Consider a computed tomography scan if surgical intervention is contemplated, as it is more sensitive and helps identify the cause of obstruction.

[n] Most malignant bowel obstructions are partial, allowing time to discuss appropriate intervention with the patient and family.

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

MALIGNANT BOWEL OBSTRUCTION

INTERVENTIONS

- Operative management[o]
  - Risks must be discussed with the patient/family (eg, mortality, morbidity, re-obstruction)
  - Improved quality of life should be the primary goal of surgical treatment
- Endoscopic management
  - Percutaneous endoscopic gastrostomy tube for drainage
  - Endoscopic stent placement
- Interventional radiology management
  - Ultrasound-guided venting tube
- Pharmacologic management
  - Use rectal, transdermal, subcutaneous, or intravenous routes of administration
  - Consider as an adjunct to an invasive procedure when invasive procedures are not an option
  - Administer Opioids - Transdermal, Subcutaneous, Intravenous
  - Administer Antiemetics: do not use antiemetics that increase gastrointestinal mobility such as metoclopramide; however, these may be beneficial in incomplete bowel obstruction
  - Administer Corticoteroids: dexamethasone 6-16 mg IV daily
  - Administer Octreotide: consider early in the diagnosis due to high efficacy and tolerability (100-300 mcg SC BID-TID or 10-40 mcg/hr continuous SC/IV infusion)
  - Administer Anticholinergics (eg, scopolamine, hyoscyamine, glycopyrrolate)
  - Administer Corticosteroids (discontinue if no improvement is noted in 3-5 days; up to 60 mg/day of dexamethasone)
- Intravenous or subcutaneous fluids
  - Consider if there is evidence of dehydration
- Enteral tube drainage
  - Usually uncomfortable
  - Increased risk of aspiration
  - Consider on a limited trial basis only if other measures fail to reduce vomiting
- Total parenteral nutrition (TPN)
  - Consider only if there is expected improvement of quality of life with life expectancy of many months to years

REASSESSMENT

Acceptable:
- Adequate control of malignant bowel obstruction symptoms
- Reduction of patient/family distress
- Acceptable sense of control
- Relief of caregiver burden
- Strengthened relationships
- Optimized quality of life
- Personal growth and enhanced meaning

→ Continue to treat and monitor symptoms and quality of life to determine whether status warrants change in strategies

→ Ongoing reassessment (See PAL-17)

Unacceptable →
- Intensify palliative care efforts
- Consult or refer to specialized palliative care services or hospice

[o]Poor prognosis criteria for surgery include: ascites, carcinomatosis, palpable intraabdominal masses, multiple bowel obstructions, previous abdominal radiation, very advanced disease, and poor overall clinical status.

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

SLEEP/WAKE DISTURBANCES INCLUDING INSOMNIA AND SEDATION

ESTIMATED LIFE EXPECTANCY

INTERVENTIONS

- Explore fears and anxiety regarding death/disease
- Evaluate type/severity of sleep-wake disturbance, including daytime impairments (eg, Epworth Sleepiness Score)
- Consider polysomnography if history is suggested of sleep-disordered breathing
- Treat contributing factors:
  - pain, depression, anxiety, delirium, and nausea
  - medication side effects or withdrawal syndromes (eg, corticosteroids, opioids, anticonvulsants, caffeine, hormones, herbals, barbiturates, benzodiazepines, alcohol, tricyclic antidepressants)
  - primary sleep disorders such as obstructive sleep apnea (OSA) and periodic limb movement disorder (PLMD)
    - CPAP/BiPAP
  - Restless leg syndrome
    - Ropinirole 0.25-4 mg PO at bedtime
- Provide cognitive-behavioral treatment
  - Includes stimulus control, progressive muscle relaxation, and sleep-hygiene education
- Provide pharmacologic therapies for refractory sleep/wake disturbance
  - Insomnia:
    - Zolpidem, 5-10 mg PO at bedtime
    - Lorazepam, 0.5-1 mg PO at bedtime
    - Trazodone, 25-100 mg PO at bedtime
    - Mirtazapine[p],7.5-30 mg PO at bedtime
  - Daytime sedation:
    - Caffeine 100-200 mg PO q 6 hrs, last dose 4 PM
    - Methylphenidate, start with 2.5-5 mg PO BID- 20 mg BID, second dose no later than noon
    - Dextroamphetamine, 2.5 mg up to 5-10 mg BID, no later than noon
    - Modafinil, 100-400 mg PO each morning

Years

Years to months →

Months to weeks

Weeks to days (Dying patient) →

- Assess patient's desire to have insomnia and sedation treated
- Adjust doses of pharmacologic therapies
  - Consider chlorpromazine, 25-100 mg PO/PR at bedtime
  - Consider quetiapine 25-50 mg PO at bedtime

REASSESSMENT

Acceptable:
- Adequate control of symptoms
- Reduction of patient/family distress
- Acceptable sense of control
- Relief of caregiver burden
- Strengthened relationships
- Optimized quality of life
- Personal growth and enhanced meaning

→ Continue to treat and monitor symptoms and quality of life to determine whether status warrants change in strategies

→ **Ongoing reassessment**

Unacceptable →
- Reevaluate contributing etiologies
- Change insomnia or antisedation therapy
- Intensify palliative care interventions
- Consult or refer to specialized palliative care services or hospice
- Consider referral for polysomnography

[p]Kim SW, Shin IS, Kim JM, Kim YC, Kim KS, Kim KM, Yang SJ Yoon JS. Effectiveness of mirtazapine for nausea and insomnia in cancer patients with depression. Psychiatry Clin Neurosci 2008;62:75-83.

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

DELIRIUM

ESTIMATED LIFE EXPECTANCY

Years / Years to months / Months to weeks →

- Assess for delirium (eg, DSM-IV criteria)
- Screen for and treat underlying reversible causes
  - Metabolic causes
  - Hypoxia
  - Bowel obstruction/ obstipation
  - Infection
  - CNS events
  - Bladder outlet obstruction
  - Medication or substance effect or withdrawal (eg, benzodiazepines, opioids, anticholinergics)
- Assess, screen for, and maximize nonpharmacologic interventions (eg, reorientation, cognitive stimulation, sleep hygiene)

Weeks to days (Dying patient) → See Interventions (PAL-21)

INTERVENTIONS

Severe delirium (agitation) →

- Avoid benzodiazepines unless patient has refractory delirium on antipsychotics
- Administer haloperidol 0.5-10 mg IV q 1-4 h prn
- Administer alternative agents: olanzapine, 2.5-7.5 mg/d PO/IV q 2-4 h prn (maximum = 30 mg/d); chlorpromazine, 25-100 mg PO/PR/IV q 4 h prn for bed-bound patients
- If agitation is refractory to high doses of neuroleptics, consider adding lorazepam, 0.5-2 mg SQ/IV q 4 h
- Titrate starting dose to optimal effect
- Consider opioid dose reduction or rotation
- Support caregivers

Mild/ moderate delirium →

- Administer haloperidol 0.5-2 mg PO BID/TID
- Administer alternative agents: risperidone, 0.5-1 mg PO BID; olanzapine, 5-20 mg PO daily; or quetiapine fumarate, 25-200 mg PO/SL BID
- Titrate starting dose to optimal effect
- Orient patient with family presence

REASSESSMENT

Acceptable:

- Adequate delirium symptom control
- Reduction of patient/family distress
- Acceptable sense of control
- Relief of caregiver burden
- Strengthened relationships
- Optimized quality of life
- Personal growth and enhanced meaning

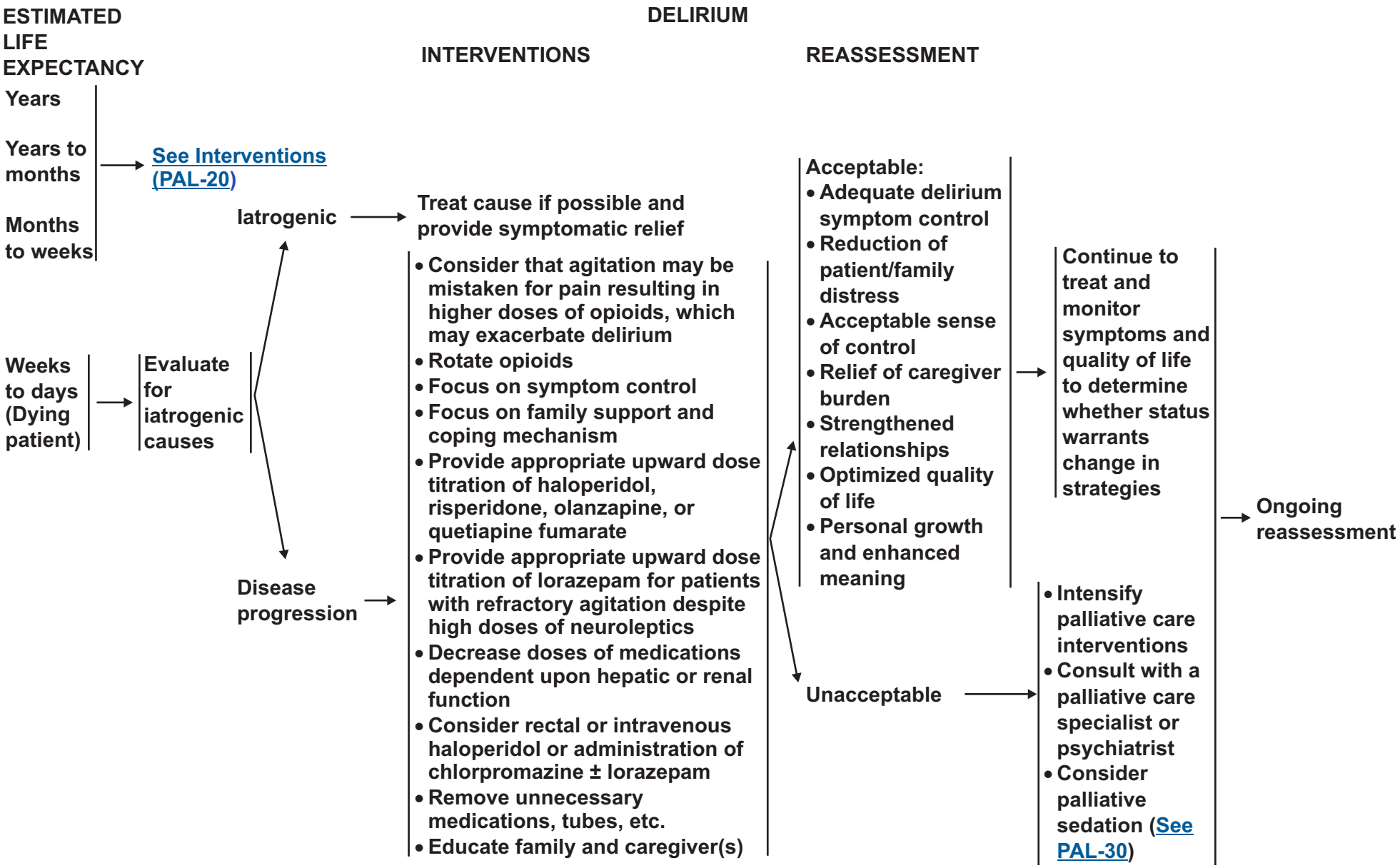
→ Continue to treat and monitor symptoms and quality of life to determine whether status warrants change in strategies → **Ongoing reassessment**

Unacceptable →

- Intensify palliative care interventions
- Consider consultation with a palliative care specialist or psychiatrist

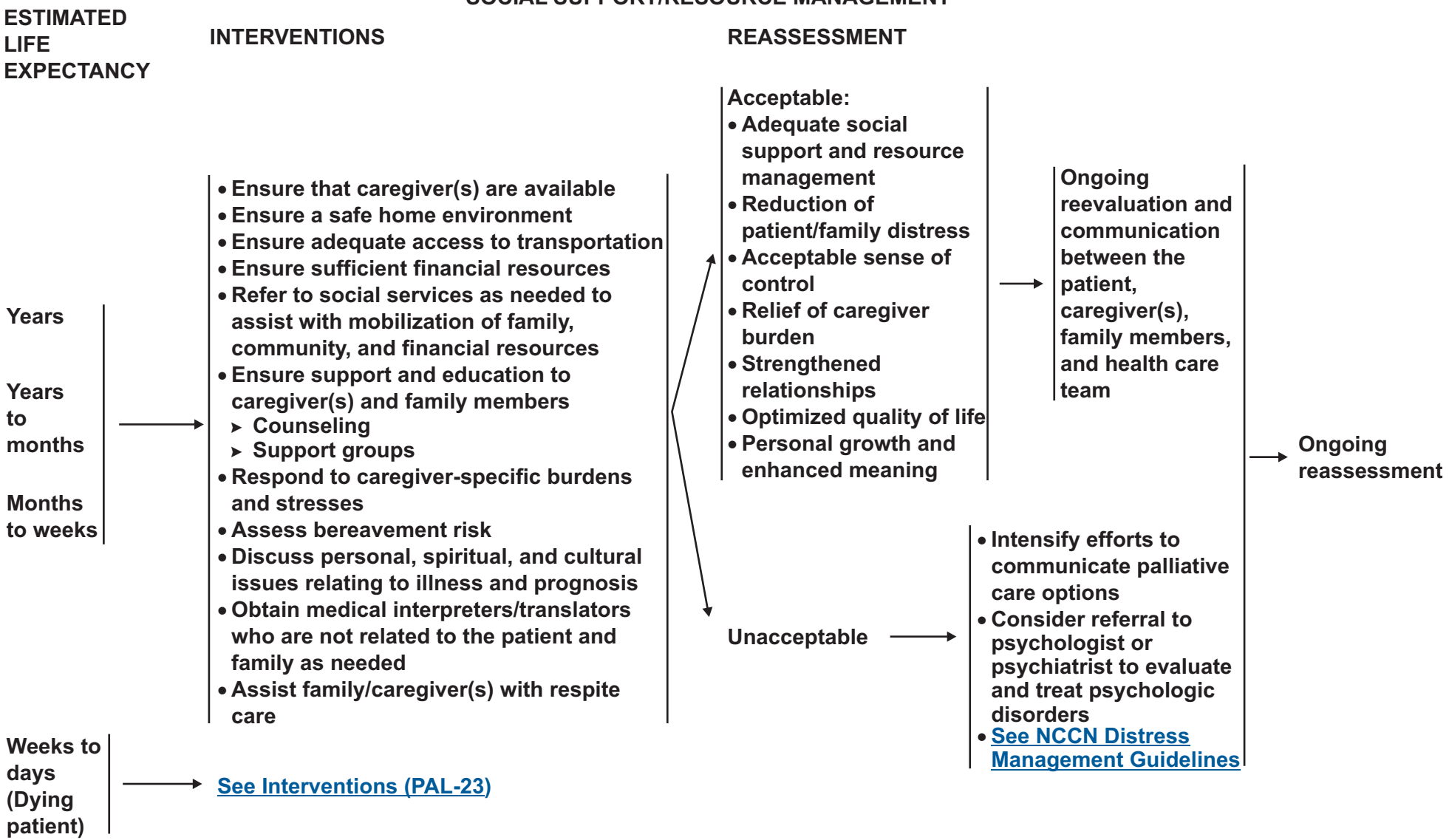
Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

DELIRIUM



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

SOCIAL SUPPORT/RESOURCE MANAGEMENT



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

SOCIAL SUPPORT/RESOURCE MANAGEMENT

ESTIMATED LIFE EXPECTANCY	INTERVENTIONS	REASSESSMENT
Years Years to months Months to weeks	→ See Interventions (PAL-22)	Acceptable: • Adequate social support and resource management • Reduction of patient/family distress • Acceptable sense of control • Relief of caregiver burden • Strengthened relationships • Optimized quality of life • Personal growth and enhanced meaning → Ongoing reevaluation and communication between the patient and health care team
Weeks to days (Dying patient)	→ • Discuss prognosis on an ongoing basis in clear, consistent language with the patient, caregiver(s), and family, including information about the natural history of the specific tumor • Evaluate and support the patient's desires for comfort • Explain the dying process and expected events to the patient, caregiver(s), and family members • Respond to caregiver-specific demands and stresses • Reassess bereavement risk • Ensure that care conforms with cultural and spiritual/religious practices • Provide emotional support and address any patient-family or intra-family conflicts regarding intervention • Consider palliative care consultation to assist in conflict resolution when the patient, family, and/or professional team do not agree on benefit/utility of interventions • Obtain medical interpreters/translators who are not related to the patient and family as needed • Determine eligibility and readiness for specialized palliative/hospice care and needs that might be best met by hospice	Unacceptable → • Reassess patient and family • Intensify palliative care efforts • Consult or refer to specialized palliative care services, hospice, or ethics committee • Consider referral to psychologist or psychiatrist to evaluate and treat psychologic disorders • See NCCN Distress Management Guidelines → Ongoing reassessment

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

GOALS AND EXPECTATIONS, EDUCATIONAL AND INFORMATIONAL NEEDS, AND CULTURAL FACTORS AFFECTING CARE FOR THE PATIENT AND FAMILY

ESTIMATED LIFE EXPECTANCY

Years

Years to months →

Months to weeks

INTERVENTIONS

- Assess patient/family understanding of expected course of disease
- Assess for decision-making capacity and need for a surrogate decision maker
- Clarify with the patient how much information she or he wishes to have and how much information should be given to the family
  - Desire for information may change and may need to be challenged as death approaches
  - Provide information about expected course of disease and anticipated care needs
  - Provide anticipatory guidance on dying process
- Facilitate decisions on providing information to family
- Determine the decision-making preferences/styles of the patient and family
  - Facilitate congruence of patient goals and expectations with those of the family
  - Recognize that the involvement of the family may change over time
- Determine the patient/family values and preferences with respect to quality of life
- Facilitate advance care planning (See PAL-26)
- Encourage the patient to review and revise personal priorities, identify "unfinished business," heal interpersonal relationships, and put affairs in order (providers should demonstrate cultural sensitivity)
- Determine eligibility and readiness for specialized palliative/hospice care and needs that might be best met by hospice
- Foster realistic expectations
- Provide clear, consistent discussion with the patient and family about prognosis on an ongoing basis
- Respect goals and needs of the patient and family regarding the dying process
- Address cultural customs and beliefs directly or through a cultural liaison
- Anticipate patient and family needs
- Provide anticipatory grief support and end-of-life education

REASSESSMENT

Acceptable:
- Reduction of patient/family distress
- Acceptable sense of control
- Relief of caregiver burden
- Strengthened relationships
- Optimized quality of life
- Personal growth and enhanced meaning

→ **Ongoing reassessment**

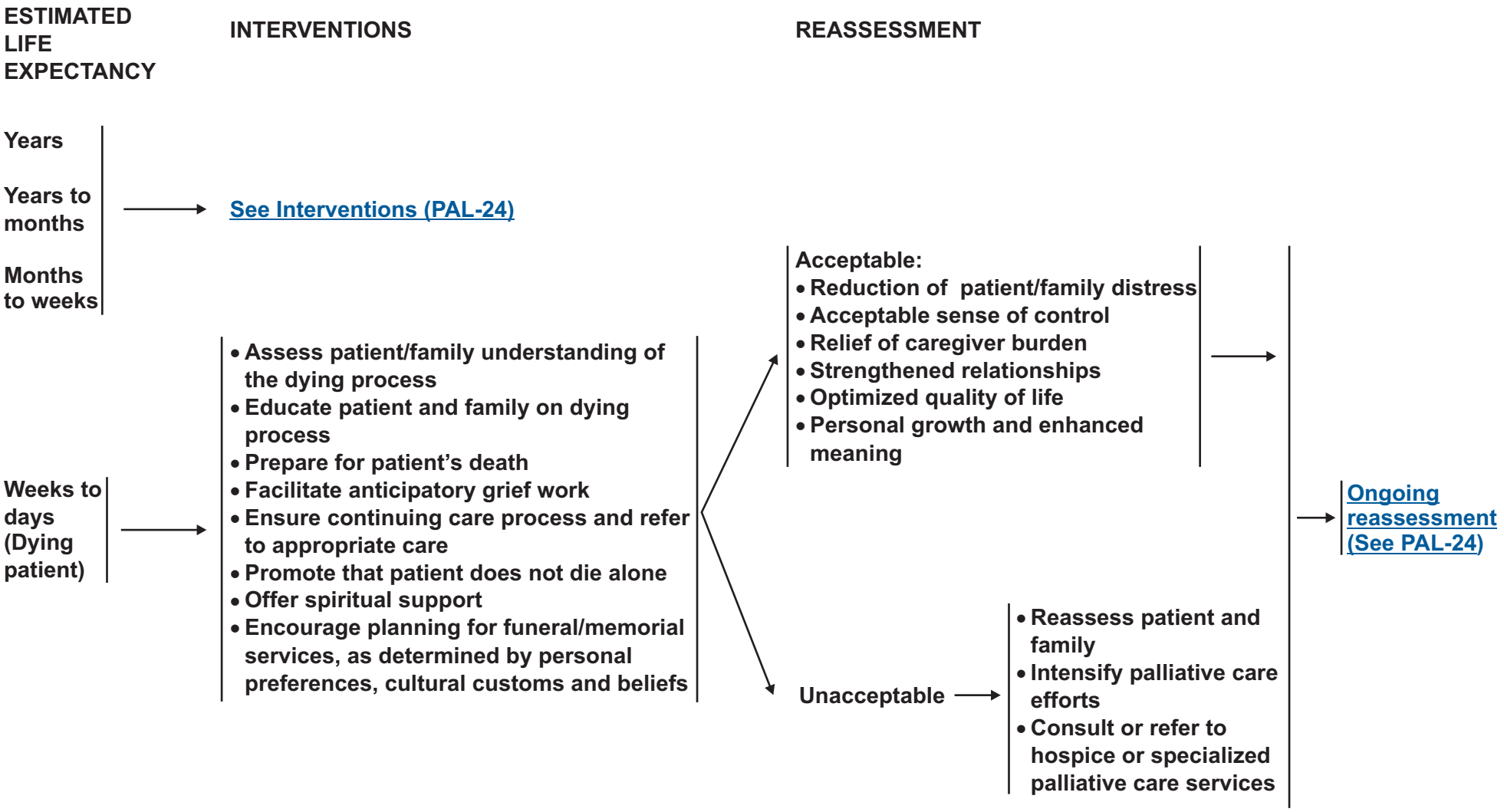
Unacceptable →
- Reassess patient and family
- Intensify palliative care efforts
- Consult or refer to specialized palliative care services or hospice

Weeks to days (Dying patient) → See Interventions (PAL-25)

See Advance Care Planning (PAL-26)

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

GOALS AND EXPECTATIONS, EDUCATIONAL AND INFORMATIONAL NEEDS, AND CULTURAL FACTORS AFFECTING CARE FOR THE PATIENT AND FAMILY



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

ADVANCE CARE PLANNING

ESTIMATED LIFE EXPECTANCY

INTERVENTIONS

- Encourage designation of health care proxy, medical power of attorney, or patient surrogate for health care
- Explore fears about dying and address anxiety
- Assess decision-making capacity and need for surrogate decision-maker
- Initiate discussion of personal values and preferences for end-of-life care
- If patient values and goals lead to a clear recommendation regarding future treatment in light of disease status, physician should make a recommendation about future care
- Document patient values and preferences and any decisions in accessible site in medical record (including MOLST/POLST if completed)
- Encourage the patients to discuss wishes with family/proxy
- Initiate discussion of palliative care options, including hospice if appropriate
- Introduce palliative care team if appropriate
- Refer to state and institutional guidelines for additional guidance

REASSESSMENT

Acceptable:

- Adequate advance care planning
- Reduction of patient/family distress
- Acceptable sense of control
- Relief of caregiver burden
- Strengthened relationships
- Optimized quality of life
- Personal growth and enhanced meaning

→ Ongoing reevaluation and communication between the patient and health care team

Unacceptable →

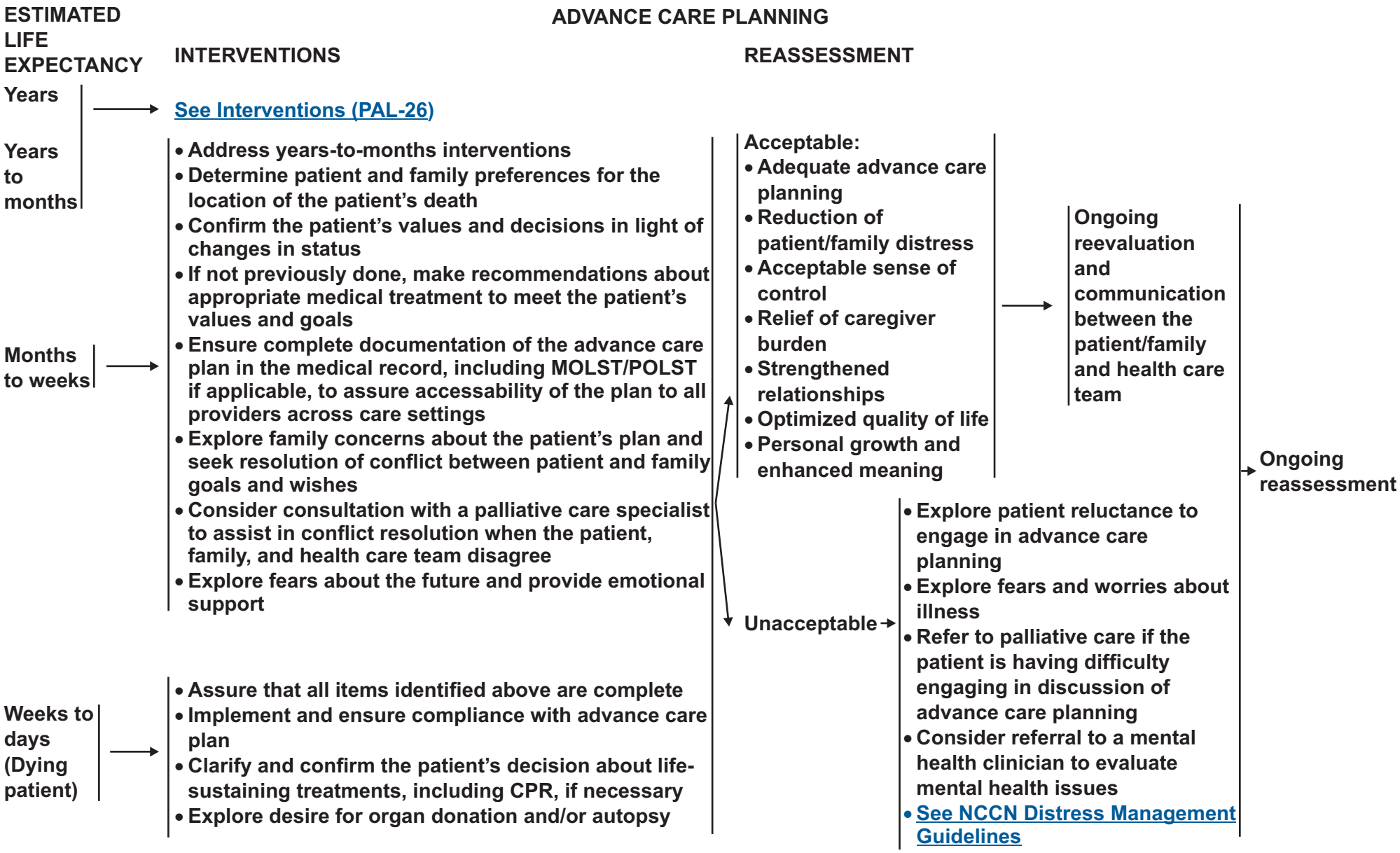
- Explore patient reluctance to engage in advance care planning
- Explore fears and worries about illness
- Refer to palliative care if the patient is having difficulty engaging in discussion of advance care planning
- Consider referral to a mental health clinician to evaluate mental health issues
- See NCCN Distress Management Guidelines

→ Ongoing reassessment

Years → **Years to months** → See Interventions (PAL-27)

Months to weeks → **Weeks to days (Dying patient)** → See Interventions (PAL-27)

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



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

RESPONSE TO REQUESTS FOR HASTENED DEATH (PHYSICIAN-ASSISTED SUICIDE, ACTIVE EUTHANASIA)

- The NCCN Palliative Care Panel believes that the most appropriate response to a request for assistance in suicide is to intensify palliative care. All such patients should be referred to a palliative care specialist. However, evaluating a patient's request for physician-assisted suicide is an important skill, even for clinicians who feel this practice is never morally acceptable. A request for hastened death often has important meanings that require exploration. Clarifying these meanings can sometimes enlarge the range of useful therapeutic options instead of providing a lethal prescription.
- Address the request explicitly. If a patient uses a euphemism for death or refers to it indirectly, ask for clarification. Do not assume that a wish for death to come soon is a wish for a lethal prescription.
- Distinguish wishing not to live in the patient's current state from wishing for a hastened death including euthanasia and physician-assisted suicide.
- Explore the reasons for the request for a hastened death, and find out "why now?"
  - Reassess symptom control.
  - Reassess psychological/psychiatric issues, especially depression, anxiety, grief, psychosis, and delirium.
  - Ask about the patient's relationship to family or other important people.
  - Ask about individual values and personal views of spiritual/existential suffering.
  - Assess for fears of caregiver burden and abandonment and re-emphasize physician commitment to the patient.
- Offer information about the natural history of the disease and explain the process of dying.
- Address the role of medical caregivers, including hospice if appropriate.
- Discuss alternatives to physician-assisted suicide such as withdrawal of life-sustaining treatment, voluntary cessation of eating or drinking, and/or sedation for refractory symptoms.
- Request a consult with a mental health professional to diagnose and treat reversible causes of psychological suffering.
- Know the local legal status of hastened death. Some patients may be confused about legal/ethical distinctions; treatment withdrawal and aggressive treatments for symptoms, such as pain, are not physician-assisted suicide. Physician-assisted suicide is legal only in Oregon, Montana, and Washington and has specific guidelines. Euthanasia is not legal in any state in the United States.
- Examine your own response as a clinician to a particular patient's request. Requests for hastened death can force clinicians to confront their own personal, professional, moral, and legal responsibilities. Dealing with an individual patient can be quite different from thinking about the issue in abstract circumstances. Consider a consultation with an ethics committee, palliative care service, or experienced colleague. These cases are usually complex and often benefit from consideration of multiple perspectives.
- Clarify the care plan. Requests for hastened death should prompt ongoing discussion and active attempts to ameliorate physical, psychological, and spiritual distress. Re-emphasize your own commitment to providing continuing care for the patient. Maintain medications for symptom control.

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

CARE OF THE IMMINENTLY DYING PATIENT

For an imminently dying patient, consider using an end-of-life care order set, which may contain physical, psychosocial, and practical interventions, including the following:

- **Physical**
  - Intensify comfort measures:
    - Implement skin safety protocol according to risk assessment, including using a pressure-relieving mattress and regularly repositioning the patient for comfort as indicated; keep skin moist; reassess wound care for comfort; and premedicate for wound care as needed
    - Provide mouth care to keep mouth/lips moist
    - Treat for urinary retention and fecal impaction
  - Ensure deactivation of implanted defibrillator and consider deactivation of implanted pacemaker
  - Discontinue unnecessary diagnostic tests and interventions such as transfusions, needle sticks, infrastructure and operations, blood glucose monitoring, oxygen saturation monitoring, and suctioning
  - Replace check of vital signs with regular (eg, every 4 h) symptom control assessments
  - Switch routes of medication administration when the oral route is no longer feasible
  - Adjust doses of medications to optimal comfort
  - Treat unclearable terminal secretions (death rattle) by changing the patient's positioning and reducing parenteral and enteral fluids.
    - For refractory secretions (See PAL-11)
  - Treat dyspnea by adjusting the dose of medication (See PAL-10)
  - Treat refractory restlessness and agitation with palliative sedation (See PAL-30)
  - Prepare to meet a request for organ donation and autopsy
- **Psychosocial**
  - Help support the patient and family to accept discontinuation of TPN and transfusions, dialysis, IV hydration, and medications that will not add to the patient's comfort
  - Consider social work and chaplain consults
  - Allow the patient and family to have uninterrupted time together
  - Ensure that the patient and family understand the signs and symptoms of imminent death and that they are supported throughout the dying process
  - Offer anticipatory bereavement support
  - Provide support to children and grandchildren
  - Encourage visits by children if consistent with family values
  - Support culturally meaningful rituals
  - Ensure that caregivers understand and will honor advance directives
  - Facilitate closure
- **Practical**
  - Mobilize in-hospital end-of-life care policies and procedures
  - Ensure that the patient's advance directives are documented and implemented
  - Recommend that the patient's wishes for resuscitation and/or do-not-resuscitate (DNR) are documented and followed
    - If the patient/family have not documented a DNR order, intensify patient/family education and counsel the family on importance of a DNR
  - Ensure privacy for the patient and family; if not at home, arrange for a private room if possible
  - Facilitate around-the-clock family presence
  - Provide the patient and family with respectful space and uninterrupted time together
  - Facilitate funeral planning

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

See After Death Interventions (PAL-31)

PALLIATIVE SEDATION

- **Confirm that the patient has refractory symptoms and is imminently dying.**
  - **Refractory symptoms are symptoms that cannot be adequately controlled despite aggressive, skilled, palliative care that does not compromise consciousness.**
  - **Imminently dying is a prognosis of hours to days confirmed by two physicians.**

- **Obtain informed consent for sedation from the patient and/or surrogate/family.**
  - **Discuss the patient's disease status, treatment goals, prognosis, and expected outcomes with the patient and/or surrogate.**
  - **Clarify that sedation will consist of the continuous administration of medications that will render the patient unconscious.**
  - **Review the ethical justification of the use of sedation with the patient/surrogate/family and members of the health care team**
    - **An ethics consult may be considered in accordance with institutional guidelines and state regulations.**
  - **Explain that consent for sedation must be accompanied by consent for:**
    - **Discontinuation of life-prolonging therapies**
    - **Withholding of cardiopulmonary resuscitation**

- **Permit reassignment of health care professionals who cannot provide sedation due to personal or professional values and beliefs as long as patient care can be safely transferred to the care of another health care professional.**

- **Select an appropriate sedative treatment plan based upon the patient's response to recent and current medications.**
  Typical sedatives used for palliative sedation parenteral infusions include:
  - **Thiopental: Initial infusion rate 20-80 mg/h; range 160-440 mg/h**
  - **Pentobarbital: Initial infusion 2-3 mg per kg load then 1-2 mg per kg/h**
  - **Midazolam: Initial infusion rate 0.4-0.8 mg/h; range 20-102 mg/h**

- **Continue current pain and symptom management control interventions.**

- **Monitor patient symptoms regularly and titrate sedatives and other medications based on response and drug/drug interactions to establish and maintain a level of sedation that relieves the patient's refractory symptoms.**

- **Provide ongoing psychosocial and spiritual support for the patient's surrogate, family, and health care professionals.**

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

DEATH	ASSESSMENT	AFTER-DEATH INTERVENTIONS
Death →	A "peaceful death": • Free from avoidable distress and suffering for the patient, family, and caregiver(s) • In general accord with the patient's and family's wishes • Consistent with clinical, cultural, and ethical standards	→ <u>For family and caregiver(s)</u> • Immediate after-death care: ▸ Provide the family time with the body ▸ Remove tubes, drains, lines, and the foley catheter unless an autopsy is planned ▸ Inform family (if not present) of death ▸ Ensure culturally sensitive, respectful treatment of the body ▸ Address survivor concerns about organ donation and/or autopsy ▸ File the death certificate, complete forms, and provide necessary information for the funeral director ▸ Offer condolences ▸ Inform other health care providers of the patient's death • Bereavement support: ▸ Formally express condolences on the patient's death (eg, card, call, letter) ▸ Refer to appropriate bereavement services within the institution or in the community ▸ Attend a debriefing meeting with the family if they desire one • Discuss cancer risk assessment and modification with family members • Identify family members at risk for complicated bereavement or prolonged grief disorder <u>For health care professionals</u> General support: • Legitimize discussion of personal issues that impact patient care • Create a climate of safety for discussion of patient deaths • Provide regular opportunities for reflection and remembering for staff through a memorial ritual After-death support: • Review medical issues related to the patient's death ▸ Explore concerns and questions regarding quality of patient care • Review the family's emotional responses to the patient's death • Review the staff's emotional responses to the patient's death ▸ Include nurses, nursing assistants, physician team members (including medical students, residents, and fellows), social workers, and chaplaincy, as appropriate ▸ Consider a bereavement ritual for staff (eg, brief reading, moment of quiet) • Identify health care professionals at risk for complicated bereavement, moral distress or compassion fatigue

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

Discussion

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.

Overview

The aim of the NCCN Palliative Care Guidelines is to help assure that each patient with cancer experiences the best quality of life that is possible throughout the illness trajectory by providing guidance for the primary oncology team. The Palliative Care Guidelines panel is an interdisciplinary group of representatives from NCCN member institutions, consisting of medical oncologists, neurologists and neuro-oncologists, anesthesiologists, psychiatrists and psychologists, internists, palliative care and pain management specialists, and geriatric medicine specialists. These guidelines were developed and updated from the collaborative efforts of these experts based on their clinical experience and available scientific evidence.

Palliative Oncology

More than 1.6 million people will be diagnosed with cancer in the United States in 2012, and more than 0.5 million people will die of the disease.[1] Global cancer rates are increasing, and there is also a rise in the number of cancer survivors living with symptoms and disabilities as a result of their disease and/or its treatment.[2] The need for comprehensive care for patients with cancer and their families is great. Approximately 16% of cancer patients being discharged from a single hospital in Germany were assessed as having palliative care needs, with the greatest need in patients with head and neck cancer, melanoma, and brain tumors.[3] More than one-third of cancer patients in a large observational cohort study reported moderate to severe symptoms in the majority of categories (pain, nausea, anxiety, depression, shortness of breath, drowsiness, well-being, loss of appetite, and tiredness) in the last weeks of life.[4]

During the past 20 years, increasing attention has been paid to quality-of-life issues in oncology.[2, 5-9] As the hospice movement has grown in this country, palliative care has developed into an integral part of comprehensive cancer care.[2, 10-14] However, most patients who receive hospice care in this country are referred too late for comprehensive palliative care to exert its full benefit, and many patients are never referred at all.[15, 16] Furthermore, administration of chemotherapy late in the course of cancer care, including in the last days of life, is growing more common,[17, 18] and oncologists have reported that they have found hospice regulations too restrictive.[19]

While palliative care previously focused on end-of-life care, there is increasing understanding that palliative care needs to be integrated earlier into the continuum of cancer care[20-24]; it needs to exist right from the time of diagnosis through survivorship and/or end-of-life care.

Palliative care should begin with the presentation of symptoms, even before the source of those symptoms has been fully determined. Building on the World Health Organization's recommended model of resource allocation in cancer care,[10] an NCCN task force recommended that palliative, symptom-modifying therapy should be provided simultaneously with disease-modifying therapy from diagnosis.[25] As the cancer progresses and anticancer therapy becomes less effective, appropriate and desired palliative care becomes the major focus of the continuing care of the patient and family.[26] Patients with increased risk for cancer should also be provided with supportive care along with risk-reduction therapies. Palliative care should continue even after the patient's death in the form of bereavement support for the patient's survivors.

Patients and families should be informed that palliative care is an integral part of their comprehensive cancer care.[27, 28] Initially, the primary oncology team (interdisciplinary team of physicians, nurses, social workers, other mental health professionals, chaplains, physician assistants, and dietitians) can provide most of the palliative care needed by the patient. Intractable symptoms or complex psychosocial problems can benefit from the inclusion of palliative care experts. As the disease progresses and the prognosis becomes a matter of months, collaboration with palliative/hospice teams is usually advised to best meet the many needs of the patient and family. Skilled, palliative care specialists and interdisciplinary palliative care teams should be readily available to provide consultative or direct care to patients/families that request or require their expertise. Clear, consistent, and empathetic communication with patient and family about the natural history of the cancer and its prognosis is at the core of effective palliative care.[29, 30] The Center to Advance Palliative Care (www.capc.org) has been established to increase the availability of quality palliative care services in hospitals and other health care settings for people with advanced illness.

In February 2012, the American Society for Clinical Oncology (ASCO) published a provisional clinical opinion, based on 7 randomized controlled trials and expert consensus.[31] The ASCO panel stated that there is substantial evidence to show that "palliative care – when combined with standard cancer care or as the main focus of care – leads to better patient and caregiver outcomes." The ASCO panel concluded that strong consideration should be given to the integration of palliative care with standard oncology care early in the course of illness for patients with metastatic cancer and/or high symptom burden.

A remarkable recent study showed that early introduction of palliative care can not only improve quality of life for patients with advanced cancer but can also improve survival.[32] A secondary analysis of this study further showed that patients receiving early palliative care were less like to receive chemotherapy in the last 60 days of life (odds ratio, 0.47; 95% CI, 0.23 to 0.99; P=0.05),[33] likely because these patients had a more accurate understanding of their prognosis that impacted decisions about their care.[34] In addition, a recent analysis of the SEER database revealed that men with advanced prostate cancer who were enrolled in hospice were less likely to receive high-intensity care, including ICU admission and inpatient stays, at the end of life.[15]

Educational programs should be provided to all health care professionals and trainees so that they can develop effective palliative care knowledge, skills, and attitudes. The number of palliative care programs in the United States is rapidly increasing. The establishment of palliative medicine as a medical subspecialty received an unprecedented level of support from at least ten cosponsoring American Board of Medical Specialties (ABMS; www.abms.org) boards

including Anesthesiology, Family Medicine, Internal Medicine, Physical Medicine and Rehabilitation, Psychiatry and Neurology, Surgery, and Pediatrics. Support for expansion of palliative medicine education has been offered by the Liaison Committee on Medical Education (LCME; www.lcme.org), which has mandated palliative medicine education for medical schools. In addition, the Accreditation Council for Graduate Medical Education (ACGME; www.acgme.org) now requires training in palliative medicine for oncology fellows, including training in pain, psychosocial care, personal awareness, and hospice care. A recent randomized controlled trial showed that specific training programs for oncologists can be effective.[35] Unfortunately, however, a recent survey of 254 hematology/oncology fellows found that palliative care education is still lacking, with only 32% of respondents reporting formal training in managing end-of-life depression and only 33% reporting explicit training in opioid rotation.[36]

Assessing outcomes and evaluating palliative cancer care is essential to ensure high-quality, evidence-based care. Lorenz et al performed a systematic review of end-of-life care and outcomes and found that many aspects of palliative care lack high-quality evidence.[37] The second edition of the Clinical Practice Guidelines for Quality Palliative Care by the National Consensus Project were published in 2009,[38] and the National Quality Forum has developed a national quality framework for evaluating palliative care programs, extending beyond terminally ill cancer patients to include a broad spectrum of patients with multiple illnesses.[39] These guidelines provide an in-depth assessment of many issues surrounding palliative care (eg, cultural, ethical, legal, physical, psychological, social, spiritual, and existential aspects of care). In addition, the American College of Physicians has developed evidence-based guidelines to improve palliative care of pain, dyspnea, and depression experienced at the end of life.[40]

In the United Kingdom in 2004, the National Consensus Project and the National Institute for Health and Clinical Excellence (NICE) issued guidance on how supportive and palliative care services should be provided for adults with cancer (www.nice.org.uk/page.aspx?o=csgsp). Some of the key recommendations are listed below:

1. Patients and their caregivers should have access to a range of specialist services that help them cope with cancer and its treatment.
2. Whenever possible, significant information should be given to patients by a senior health professional that has received advanced level training and is assessed as being an effective communicator.
3. Good quality information should be available free of charge to help people affected by cancer make decisions about their care.

ASCO recently published a statement on individualized care for patients with advanced cancer.[8] While significant improvements over the past decade were noted (eg, improvements in palliative care education and training for oncologists and an increase in hospital-based palliative care programs and community-based hospice organizations), the statement points out that conversations with patients about their palliative needs are still happening too late in the progression of their disease. Some of the key elements of individualized care listed in the report state that patients should be given

- enough information to enable them to make informed choices regarding their treatment
- encouragement to focus on symptom-directed palliative care when disease-directed therapies fail
- the opportunity to participate in clinical trials that may improve their outcome or that of future patients

- the opportunity to die with dignity and peace of mind.

Other resources that may be useful for patients, their caregivers, and/or clinicians are listed in Table 1, below.

Palliative Care Standards

In August 2011, the Commission on Cancer (CoC) of the American College of Surgeons (ACS) released new accreditation standards for hospital cancer programs (http://www.facs.org/news/2011/coc-standards0811.html).[41] Their patient-centered focus requires that patients have access to palliative and hospice care, psychosocial support, and pain management – either on-site or by referral. The standards also state that palliative care should be provided by an interdisciplinary team of medical and mental health professionals, social workers, and spiritual counselors and should be available beginning at the time of diagnosis and continuously throughout treatment, surveillance, and bereavement.

Palliative Care Guidelines

The NCCN Palliative Care Guidelines were developed to facilitate the appropriate integration of palliative care into oncology practice. The guidelines outline procedures for screening, assessment, palliative care interventions, reassessment, and after-death care. The panel chose to focus on the needs of patients in their last 12 months of life. The panel chose this period to distill the content of textbooks and curricula into guidelines that could facilitate clinical decision-making in the same way that NCCN disease-oriented and symptom-oriented guidelines have, although patients and families can certainly benefit from palliative care integrated throughout the illness trajectory.

The guidelines define palliative care as a special kind of patient and family-centered health care that focuses upon effective management of pain and other distressing symptoms, while incorporating psychosocial and spiritual care according to patient/family needs, values, beliefs, and cultures(s). The goals of palliative care are to anticipate, prevent, and reduce suffering and to support the best possible quality of life for patients and their families, regardless of the stage of the disease or the need for other therapies. Palliative care begins at diagnosis and should be delivered concurrently with disease-directed, life-prolonging therapies and should 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 initiated by the primary oncology team and then augmented by collaboration with an interdisciplinary team of palliative care experts.

Palliative Care Screening

The primary oncology team should screen all patients at every visit for (1) uncontrolled symptoms, (2) moderate to severe distress related to cancer diagnosis and therapy, (3) serious comorbid physical, psychiatric, and psychosocial conditions, (4) life expectancy of 6 months or less, (5) patient or family concerns about the course of disease and decision-making, and/or (6) a specific request for palliative care by the patient or family. Patients who meet these screening criteria should undergo a full palliative care assessment.

Patients who do not meet these screening criteria should be re-screened at the next visit. In addition, the oncology team should inform patients and their family members about the role and benefits of palliative care services. Anticipation of palliative care needs and

prevention of symptoms should also be discussed, and conversations regarding advance care planning should be initiated.

Palliative Care Assessment

Patients who meet screening criteria (see above) should undergo a comprehensive palliative care assessment by their primary oncology team evaluating the benefits and risks of anticancer therapy; physical symptoms; psychosocial or spiritual distress; personal goals and expectations; educational and informational needs; and cultural factors affecting care.[5-7]

Benefits and Risks of Anticancer Therapy

Assessment of the benefits and risks of anticancer therapy is based on the existing NCCN disease-specific guidelines (the most recent version of all guidelines can be found on the NCCN Web site at www.nccn.org). Special attention should be given to the natural history of the specific tumor; the potential for response to further treatment; the meaning of anticancer therapy to patient and family; the potential for treatment-related toxicities including impairment of vital organs and performance status; and serious comorbid conditions. Specific recommendations regarding anticancer therapy for patients with various life expectancies are discussed in 'Palliative Care Interventions,' below.

Physical Symptoms

The most common symptoms that need to be assessed are pain, dyspnea, anorexia, cachexia, nausea, vomiting, constipation, malignant bowel obstruction, fatigue, weakness, asthenia, insomnia, daytime sedation, and delirium. Palliative interventions for these symptoms are discussed individually below.

Psychosocial Distress

Assessment of psychosocial distress should focus on illness-related distress and psychosocial, spiritual, or existential issues according to the NCCN Clinical Practice Guidelines in Oncology for Distress Management (for the most recent version of these guidelines, visit the NCCN Web site at www.nccn.org). Special problems with social support and resources (ie, home, family, community, or financial issues) must also be assessed. Recommendations for the management of psychosocial distress can be found in the NCCN Distress Management guidelines and below.

Personal Goals and Expectations

Patients and their families should also be asked about their personal goals and expectations. Their priorities for palliative care, including their goals and perceived meaning of anticancer therapy and the importance they place on quality of life should be assessed. Goals and expectations that might be better met by the hospice model of palliative care should be identified.

Educational and Information Needs and Cultural Factors Affecting Care

The values and preferences of patients and families about information and communication should also be assessed. The oncology team should inquire about cultural factors affecting care and perceptions of the patient/family regarding the patient's disease status.

Consultation with Palliative Care

Criteria for consultation with a palliative care specialist are based on patient characteristics, social circumstances, and anticipatory bereavement issues. The oncology team should consider consultation in the case of patients with limited treatment options; refractory non-pain symptoms or a high symptom burden; history of allergies or adverse effects to multiple palliative interventions; complicated ICU

admissions; a high distress score (≥4; see the NCCN Distress Management Guidelines); cognitive impairment; severe comorbid conditions; or communication barriers. In addition, consultation with palliative care specialists should be considered for those at high risk for poor pain control; those who make requests for hastened death; and/or those who are unable to engage in advance care planning. Social circumstances or anticipatory bereavement issues that indicate a need for referral for consultation with a palliative care specialist include family/caregiver limitations, inadequate social support, financial limitations, limited access to care, family discord, intensely dependent relationships, financial limitations, limited access to care, patient's concern regarding care of dependents, spiritual or existential distress, and/or unresolved or multiple prior losses.

Palliative Care Interventions

The oncology team should initiate palliative 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 problems to improve their quality of life and survival.[31, 32] Referrals should be made as needed to mental health and social services, health care interpreters, hospice services, or other specialists. Finally, the oncology team can be helpful in mobilizing community support through religious organizations, schools, or community agencies.

The panel divided patients into 3 groups to address the effect of life expectancy on the delivery of palliative care interventions: 1) patients with years to months to live, 2) patients with months to weeks to live, and 3) dying patients in their final weeks to days. Patients in their final hours of life are referred to as *imminently dying* and may require special interventions. The panel recognizes the lack of precision in estimating life expectancy but believes that this delineation will be useful for the delivery of appropriate palliative care interventions. The patient and family's personal, spiritual and existential, cultural, and religious goals and expectations may change throughout these timeframes. Optimal provision of palliative care requires ongoing reassessment and modification of strategies, as well as ongoing communication between the patient, family, and health care team.

Indicators that patients are in their last 6 months of life include decreased performance status (ECOG score ≥3; KPS score ≤50), hypercalcemia, central nervous system metastases, delirium, superior vena cava syndrome, spinal cord compression, cachexia, malignant effusions, liver failure, kidney failure, or other serious comorbid conditions. Many patients with stage IV cancers, especially those with stage IV lung cancer, pancreatic cancer, and glioblastoma multiforme, would benefit from palliative care beginning at diagnosis, because expected survival is limited.

For patients whose life expectancy is "years to months" or "months to weeks," it is important to determine how much information a patient wishes to know and how much of that information should be shared with the patient's family. Patients will also require answers to any questions about what to expect in the next few months and anticipatory guidance on the dying process. In addition, determining the decision-making styles of patients and their families helps facilitate congruence of a patient's goals and expectations with those of the family. Clinicians should also determine the patient's assessment of the relative importance of quality of life compared with length of life. Patients should be assisted in reviewing and revising their life priorities,

resolving their unfinished business, and putting their financial and personal affairs in order.

Dying patients may wish to prepare for death and to help prepare family members to go on without them. Both patients and families benefit from education on the dying process. Families should be guided through their anticipatory grief, and arrangements should be made to ensure that the patient's and family's needs and goals regarding the dying process are respected. Planning to ensure continuing care and referrals to appropriate care is important. Arrangements should be available to ensure that the patient does not die alone unless that is the patient's preference.

Clinicians should discuss the prognosis with patients and their families clearly and consistently to help them develop realistic expectations. Information about the natural history of the specific tumor and the realistic outcomes of anticancer therapy should be included in the discussion. Many investigators have shown that seriously ill middle-aged and older patients tend to be more optimistic and less accurate about their prognosis than their physicians; such misunderstanding of the situation can affect their preferences for cardiopulmonary resuscitation and for life-extending measures.[42]

Spiritual, existential, and cultural issues are often best addressed through collaboration with pastoral care counselors, professional translators, the patient's personal clergy, and representatives from the patient's cultural community. Religious and cultural issues surrounding the beliefs and practices near the time of death must be anticipated and carefully managed.[43] Finally, social and spiritual support and resource management interventions should be provided to ensure a safe end-of-life care environment, a competent primary caregiver, and access to necessary medications and treatments. Providers must be sensitive to cultural values that may influence the best way for this information to be presented and discussed.

Palliative care interventions for managing specific symptoms and the benefits and risks of anticancer therapy are discussed below as outlined in the algorithms. Additional palliative care interventions for other symptoms will be developed as deemed necessary.

Anticancer Therapy

Patients who have years to months to live and a good performance status are likely to be interested in continuing anticancer therapy to prolong survival and reduce cancer-related symptoms.[44-47] Anticancer therapy may be conventional evidence-based treatment as outlined in the NCCN disease-specific guidelines (available on the NCCN Web site at www.nccn.org) or treatment in the context of a clinical trial. In some of the advanced-stage cancers, chemotherapy may be superior to best supportive care and may prolong survival.[48, 49] Furthermore, patients with advanced non-small cell lung cancer who are not eligible for systemic chemotherapy may benefit from targeted therapies that are effective for relieving symptoms, maintaining stable disease, and improving quality of life without the adverse events that may be associated with cytotoxic cancer therapies.[50] Physicians, patients, and their families should discuss intent, goals, range of choices; benefits and risks of anticancer therapy; and possible effects on quality of life. In addition, the oncology team should prepare the patient psychologically for possible disease progression.

Patients with months to weeks to live should be provided with guidance regarding the anticipated course of the disease. These patients are typically tired of therapy, homebound, and more concerned about the side effects of more treatment. The focus of treatment for these patients shifts from prolonging life towards maintaining quality of life. These

patients should consider potential discontinuation of anticancer treatment and be offered best supportive care, including referral to palliative care or hospice.[51, 52] To avoid demeaning the value of end-of-life care, palliative care should not be described as "just hospice."

In general, patients with weeks to days to live (ie, dying patients) should not be given anticancer therapy, but should be given intensive palliative care focusing on symptom control and preparation for the dying process.

Symptoms

Special considerations in the implementation of these guidelines based on life expectancy are delineated in the algorithms. The major focus of these special considerations is the withholding and withdrawal of aggressive interventions, prevention and elimination of side effects associated with pharmacological pain management, the acceptance of loss of function for the sake of relief of symptoms, and the treatment of the unique symptoms of patients in their final hours of life. With regard to symptoms, the control of pain, dyspnea, anorexia/cachexia, nausea and vomiting, constipation, malignant bowel obstruction, fatigue, delirium, and psychological distress is fundamental and discussed in detail below.

Pain

See the NCCN Clinical Practice Guidelines in Oncology on Adult Cancer Pain (for the most recent versions of these guidelines, visit the NCCN Web site at www.nccn.org). In addition, it is important to note that dying patients in their last weeks of life have several specific requirements. For instance, opioid dose should not be reduced solely for decreased blood pressure, respiration rate, or level of consciousness. In fact, opioids can be titrated aggressively for moderate/severe acute/chronic pain.[53] In addition, palliative sedation can be considered for refractory pain (see below) following consultation with pain management/palliative care specialists.

Dyspnea

Dyspnea is one of the most common symptoms in patients with advanced lung cancer.[54] The American Thoracic Society consensus statement defines dyspnea as "a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity."[55]

Symptom intensity should first be assessed in all patients. Symptom intensity in non-communicative patients with weeks to days to live should be assessed using other distress markers of dyspnea. Next, underlying causes or comorbid conditions should then be treated using chemotherapy or radiation therapy; therapeutic procedures for cardiac, pleural, or abdominal fluid[56-58]; bronchoscopic therapy; or bronchodilators, diuretics, steroids, antibiotics, or transfusions.

Both pharmacologic and non-pharmacologic interventions have been assessed for management of dyspnea. A recent review concluded that there is little definitive data to evaluate the effectiveness of dyspnea interventions and that randomized controlled trials are needed.[59] Other reviews have determined that there is sufficient data to make treatment recommendations.[57, 60] Pharmacologic interventions include opioids or benzodiazapines.[57, 61-64] Scopolamine, atropine, hyoscyamine, and glycopyrrolate are options to reduce excessive secretions associated with dyspnea.[65-69] Glycopyrrolate does not effectively cross the blood brain barrier,[70] and thus is less likely than the other drug options to cause delirium.[71, 72] Scopolamine can be administered subcutaneously or transdermally; physicians should be aware that the onset of benefit for transdermal scopolamine patches is about 12 hours,[73] and they are thus not an appropriate choice for imminently dying patients. A

subcutaneous injection of scopolamine can be administered when the patch is applied or if control of secretions is inadequate. Benzodiazepines can be tried for treatment of dyspnea when other options have failed; the beneficial effect of benzodiazepines on breathing in patients with advanced cancer is small.[64]

A recent study revealed that nebulized fentanyl reduces the intensity and unpleasantness of dyspnea in patients with chronic obstructive pulmonary disease (COPD).[74] Nebulized fentanyl has not yet been studied in cancer patients, but can be considered in patients who do not respond well to the other interventions in these guidelines.

Non-pharmacologic interventions include the use of handheld fans directed at the face. A randomized, controlled, crossover trial demonstrated that breathlessness was reduced in patients when they directed a handheld fan toward their faces.[75] A time-limited trial of mechanical ventilation, as clinically indicated, and/or oxygen therapy for hypoxia may also be beneficial.

As life expectancy decreases, the role of mechanical ventilation and oxygen diminishes, and the role of opioids, benzodiazepines, glycopyrrolate, and scopolamine increases.

Anorexia / Cachexia

Cachexia is physical wasting with loss of skeletal and visceral muscle mass and is very common among cancer patients.[76, 77] 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.[76, 77] 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 anti-cancer treatment, increased treatment toxicity, delayed treatment initiation, early treatment termination, and shorter survival.[76, 77]

Treatment includes the relief of symptoms that interfere with food intake (eg, depression, pain, constipation, nausea/vomiting), metoclopramide for early satiety, and the use of appetite stimulants (megestrol acetate, medroxyprogesterone acetate, or corticosteroids) when increased appetite is an important aspect of quality of life.[57, 60, 78-80] The panel cautions that megestrol acetate can cause blood clots in rare cases. Nutrition consultation should also be considered, because calory-dense, high-protein supplementation has demonstrated some efficacy for weight stabilization,[57, 76, 81-83] although some studies show nutritional intervention to be ineffective.[84] Nutrition support, including enteral and parenteral feeding as appropriate, should also be considered when the disease or treatment affects the ability to eat and/or absorb nutrients.[85]

The goals and intensity of nutritional support change as life expectancy is reduced to weeks to days. Family members should be informed of alternate ways to care for dying patients. Overly aggressive enteral or parenteral nutrition therapies can actually increase the suffering of dying patients.[85-88] In terms of hydration and nutrition, palliative care in the final weeks of life typically includes treating dry mouth and thirst, and providing education and support to the patient and family regarding the emotional aspects of withdrawal of nutritional support.

Nausea and Vomiting

Chemotherapy-induced nausea and vomiting (CINV) has a major impact on a patient's quality of life.[89] Nausea and vomiting induced by chemotherapy or radiation therapy should be managed as outlined in the NCCN Clinical Practice Guidelines in Oncology on Antiemesis (for the most recent version of these guidelines, visit the NCCN Web site at

www.nccn.org). Patients can also experience nausea and vomiting unrelated to chemotherapy and radiation, resulting from gastric outlet obstruction, bowel obstruction, constipation, opioid use, or hypercalcemia.[90] These causes should be identified and treated. Many medications can also cause nausea and vomiting, and blood levels of possible culprits, such as digoxin, phenytoin, carbamazepine, and tricyclic antidepressants, should be checked.[91, 92]

Non-specific nausea and vomiting can be managed with dopamine receptor antagonists (eg, prochlorperazine, haloperidol, metoclopramide) or benzodiazepines (anxiety-related nausea).[93, 94] Persistent nausea and vomiting can be treated by titrating dopamine receptor antagonists to maximum benefit and tolerance.[95, 96] For persistent nausea, adding 5-HT3 (5-hydroxytryptamine 3) receptor antagonists[97, 98] and/or anticholinergic agents and/or antihistamines,[99] corticosteroids,[99, 100] continuous or subcutaneous infusion of antiemetics, antipsychotics (eg, olanzapine or haloperidol),[101] and/or cannabinoids can also be considered.[102] Opioid rotation may also help alleviate symptoms.[103] Alternative therapies (eg, acupuncture, hypnosis, or cognitive behavioral therapy) can also be considered.[104-106] Palliative sedation (see below) can be considered as a last resort if intensified efforts by specialized palliative care or hospice services fail.

A recent systematic review assessed the level of evidence for antiemesis unrelated to chemotherapy.[107] While the authors concluded that antiemetic recommendations have moderate to weak evidence at best, the strongest evidence supports the use of metoclopramide; studies of multidrug combination therapies do not support their effectiveness.

Constipation

Constipation occurs in approximately 50% of patients with advanced cancer and most patients treated with opioids.[108] Although several drugs including antacids, anticholinergic drugs (antidepressants, antispasmodics, phenothiazines, and haloperidol), and antiemetics are known to cause constipation,[109] opioid analgesics are most commonly associated with constipation. Opioid-induced constipation should be anticipated and treated prophylactically with a stimulating laxative to increase bowel motility with or without stool softeners.[110] While there is little evidence on which is the best initial bowel regimen in cancer patients, one small study compared the use of senna alone versus a senna-docusate combination. The results demonstrated that the addition of the stool softener docusate was not necessary.[111] Increasing fluid intake, dietary fiber, and physical activity should also be encouraged, when appropriate.

If constipation is present, the cause and severity must be assessed. Impaction, obstruction, and other treatable causes, such as hypercalcemia, hypokalemia, hypothyroidism, and diabetes mellitus, should be assessed and treated. Constipation may also be treated by adding bisacodyl 10-15 mg, 2 to 3 times daily with a goal of 1 non-forced bowel movement every 1-2 days. If impaction is observed, glycerine suppositories may be administered or manual disimpaction performed.

If constipation persists, adding other laxatives may be considered, such as rectal bisacodyl once daily or oral polyethylene glycol, lactulose, magnesium hydroxide, or magnesium citrate. If gastroparesis is suspected, the addition of a prokinetic agent, such as metoclopramide, may be considered. Recent studies have shown that methylnaltrexone, a peripherally acting antagonist of μ-opioid receptors, helps relieve opioid-induced constipation while maintaining pain control.[112, 113] Based

on these results, the NCCN Palliative Care panel recommends considering 0.15 mg per kilogram of body weight of methylnaltrexone every other day (no more than once a day) for patients experiencing constipation that has not responded to standard laxative therapy. Methylnaltrexone should not be used in patients with a post-operative ileus or mechanical bowel obstruction.

Malignant Bowel Obstruction

Malignant bowel obstructions are usually diagnosed clinically and confirmed with radiography. For patients with years to months to live, surgery following CT scan is the primary treatment option. While surgery can lead to improvements in quality of life, surgical risks should be discussed with patients and families.

Although surgery is the primary treatment for malignant obstruction, some patients with advanced disease or patients in generally poor condition are unfit for surgery and require alternative management to relieve distressing symptoms. In these patients, medical management can include pharmacologic measures, parenteral fluids, endoscopic management, and enteral tube drainage. Use of octreotide is highly recommended early in the diagnosis because of its high efficacy and tolerability.[114] Medical measures such as opioid analgesics, anticholinergic drugs, corticosteroids, and antiemetics may be used alone or in combination to relieve symptoms.[115, 116] Antiemetics that increase gastrointestinal mobility such as metoclopramide should not be used in patients with complete obstruction, but may be beneficial when obstruction is partial.

A venting gastrostomy tube (inserted by interventional radiology, endoscopy, or surgery), a percutaneous endoscopic gastrostomy tube, or an endoscopically placed stent can also palliate symptoms of malignant bowel obstruction.[117, 118] Total parenteral nutrition (TPN) can be considered to improve quality of life in patients with a life expectancy of years to months.

Fatigue / Weakness / Asthenia

See NCCN Cancer-Related Fatigue Guidelines (for the most recent version of these guidelines, visit the NCCN Web site at www.nccn.org).

Sleep / Wake Disturbances

Patients with cancer often suffer from insomnia or daytime sedation.[119, 120] Patients should first be evaluated for sleep/wake disturbances using, for example, the Epworth sleepiness scale.[121] If patients have a history of sleep-disordered breathing (eg, excessive snoring, gasping for air, observed apneas, frequent arousals, sudden involuntary movement of arm or legs during sleep, or unexplained daytime drowsiness), polysomnography should be considered. Polysomnography should also be considered for patients with head and neck cancers, because obstructive sleep apnea (OSA) is prevalent in patients with this disease.[122, 123] Primary sleep disorders, such as OSA and periodic limb movement disorder (PLMD), should be treated with continuous positive-airway pressure (CPAP) or biphasic positive airway pressure (BiPAP).[124] Restless leg syndrome, if present, can be treated with ropinirole.

Fears and anxiety regarding death and disease should be explored, and other contributing factors to the sleep/wake disturbance should be treated, including pain, depression, anxiety, delirium, and nausea. Cognitive behavioral therapy may be effective in treating sleep/wake disturbances in patients with cancer.[60, 125-127]

For refractory insomnia, pharmacologic management includes the short-acting benzodiazepine lorazepam, the non-benzodiazepine zolpidem, and sedating antidepressants such as trazodone and

mirtazapine.[128] The panel suggests that mirtazapine may be especially effective in patients with depression and anorexia. Benzodiazepines should be avoided in older patients and in patients with cognitive impairment, because they have been shown to cause decreased cognitive performance.[129]

For refractory daytime sedation, the guidelines suggest several options. The central nervous system stimulant methylphenidate should be given with a starting dose of 2.5-5mg PO with breakfast, proceeding to 10mg PO with breakfast and an additional 10mg PO with lunch. Doses can be escalated as needed as patients get sicker.[130] Another option for refractory daytime sedation is the psychostimulant modafinil, which has been approved in adults for excessive sleepiness associated with obstructive sleep apnea/hypopnea syndrome (OSAHS), shift work sleep disorder (SWSD), and narcolepsy.[131] The panel also recommends caffeine and dextroamphetamine as additional options for refractory daytime sedation. The last dose of caffeine should be given no later than 4PM.

Dying patients should be assessed for their desire to have their insomnia or sedation treated. The doses of their pharmacologic therapies can be adjusted as appropriate. The addition of an anti-psychotic drug (chlorpromazine or quetiapine) can be considered in patients whose insomnia is refractory.

Please also see the NCCN Adult Cancer Pain and the NCCN Cancer-Related Fatigue guidelines for their discussions on sleep/wake disturbances.

Delirium

Delirium should be assessed using the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria.[132] Reversible causes should be identified and treated appropriately. Non-pharmacological interventions (eg, reorientation, cognitive stimulation, and sleep hygiene) should be maximized before pharmacological interventions are used. In particular, benzodiazepines should be avoided unless the patient has refractory delirium on antipsychotics. The symptoms of moderate delirium can be controlled with oral haloperidol, risperidone, olanzapine, or quetiapine fumarate.[133-135] The symptoms of severe delirium (ie, agitation) should be controlled with antipsychotic, neuroleptic drugs such as haloperidol, olanzapine, or chlorpromazine.[136] Because of its hypotensive side effect, intravenous chlorpromazine should only be used in bed-bound patients. A benzodiazepine, such as lorazepam, may be added for agitation that is refractory to high doses of neuroleptics.[137] The presence of therapeutic levels of neuroleptics usually prevents the paradoxical excitation sometimes seen when delirious patients are given lorazepam. The dosages of these symptom-control medications should be titrated to optimal relief. Opioid dose reduction or rotation can also be considered for patients with severe delirium. Caregivers should be supported in caring for their loved one and coping with this distressing condition.

Delirium in patients with advanced cancer and limited life expectancy may shorten prognosis.[138] In these patients, iatrogenic causes should be eliminated whenever possible. Opioid rotation can be considered (see NCCN Adult Cancer Pain Guidelines; for the most recent version of these guidelines, visit the NCCN Web site at www.nccn.org) if the delirium is believed to be caused by neurotoxicity of the current opioid. If delirium is a result of disease progression, palliative care must be focused on symptom control and family support. Neuroleptic and benzodiazepine medications should have their dose increased and/or their route of administration changed to ensure adequate delirium symptom control.[139] Unnecessary medications and tubes should be

removed. For refractory delirium in dying patients, palliative sedation can be considered following consultation with a palliative care specialist and/or psychiatrist (see below).

Please also see the NCCN Distress Management guidelines for further discussion of delirium in patients with cancer (for the most recent version of these guidelines, visit the NCCN Web site at www.nccn.org).

Psychosocial Distress – Social Support / Resource Management
For distress related to psychological or psychiatric complications and spiritual or existential crisis, please see the NCCN Distress Management guidelines (for the most recent version of these guidelines, visit the NCCN Web site at www.nccn.org).

For patients with estimated life expectancy ranging from years to months experiencing psychosocial distress, social support/resource management should be offered. Patients should be cared for in a safe environment with available caregivers. In addition, it is important to ensure that the patient has adequate financial resources and to refer to social services as needed. Support and education should be provided to the caregivers and family members. Personal, spiritual, or cultural issues related to the patient's illness and prognosis should be discussed. Bereavement risk should be assessed. If language is a barrier, a professional health care interpreter, who is not related to the patient or family, should be available for patients, caregivers, and families as needed.

In a dying patient with an estimated life expectancy of weeks to days, the patient's desires for comfort should be evaluated and supported. The process of dying and the expected events should be explained to the patient, caregivers, and family members. Bereavement risk should be reassessed. Patients and family members should be provided with emotional support to address any intra-family conflict regarding palliative care interventions. Eligibility and readiness for specialized palliative/hospice care should be determined.

Advance Care Planning
The oncology team should initiate discussions of personal values and preferences for end-of-life care while patients have a life expectancy of years to months. Recent studies have shown that these discussions happen too late in the trajectory of disease, often during acute hospital care and often with health professionals other than the primary oncologist.[140]

Advance care planning should include an open discussion about palliative care options, such as hospice; personal values and preferences for end-of-life care; the congruence between the patient's wishes/expectations and those of the family/health care team; and information about advance directives. Patients should be asked if they have completed any advance care planning such as living wills, powers of attorney, or delineation of specific limitations regarding life-sustaining treatments including cardiopulmonary resuscitation, mechanical ventilation, and artificial nutrition/hydration. The patient's values and preferences and any decisions should be documented in the medical record, including MOLST or POLST (Medical Orders for Life Sustaining Treatment or Physician Orders for Life Sustaining Treatment) if completed.

When the patient's life expectancy is reduced to months to weeks, the oncology team should actively facilitate completion of appropriate advance directives and ensure their availability in all care settings. MOLST/POLST should be documented and accessible to all providers across care settings. The team should also confirm the patient's values and decisions in light of changes in status. Palliative care consultation

can be considered to assist in conflict resolution when the patient, family, and/or medical professional team do not agree on the benefit/efficacy of interventions.

Where the patient wants to die should be determined. Dying in a hospital can be traumatic for patients and their families. A recent prospective study showed that patients dying in an intensive care unit had higher levels of physical and emotional distress compared with patients dying at home or in hospice and that caregivers of these patients had greater incidence of prolonged grief disorder.[141] In fact, most cancer patients wish to die at home. According to the National Home and Hospice Care Survey, the number of adult cancer patients using hospice care tripled during 1991-1992 through 1999-2000.[142] Still, some patients request to remain in a facility for end-of-life care, and providing palliative care services has been shown to decrease deaths in intensive care units.[143]

If advance care plans have not been completed, the oncology team should explore the patient's reluctance to engage in advance care planning and refer to palliative care if needed.

In patients with a life expectancy of only weeks to days, the patient's decision regarding cardiopulmonary resuscitation and other life-sustaining treatments must be clarified and confirmed. The desire for organ donation and/or autopsy must also be explored with the patient. Overall, the oncology team must implement and ensure compliance with the patient's advance care plan.

Palliative Care Reassessment

The outcome measures for these guidelines are much more difficult to define than those for NCCN disease-specific guidelines. The panel reviewed end-of-life care outcomes from several surveys of North American citizens.[144-147] The panel chose a modified version of Singer's outcomes until more precise outcome measures are available. Acceptable palliative care should provide the following: 1) adequate pain and symptom management, 2) reduction of patient and family distress, 3) acceptable sense of control, 4) relief of caregiver burden, 5) strengthened relationships, and 6) optimized quality of life, personal growth, and enhanced meaning. The panel added 'having an advance care plan in progress' as part of the criteria for acceptable outcome. Research is ongoing regarding better ways to measure "dying well."[148]

All patients should be reassessed regularly, and effective communication and information sharing must exist between the patient, caregivers, and health care providers. Patients and family members benefit most from ongoing discussions about the natural history of the disease and prognosis in clear, consistent language. If the interventions are unacceptable upon reassessment, the oncology or palliative care team should intensify palliative care efforts and reassess the patient and family situation. The oncology team should also consult specialized palliative care services, hospice, or ethics committee. Referral to a psychiatrist or psychologist to evaluate and treat undiagnosed psychiatric disorders, substance abuse, and inadequate coping mechanisms should be considered. If psychosocial distress persists, palliative care options should be intensified, and the patients should be managed according to the NCCN Distress Management Guidelines.

Reassessment should be ongoing, with continuation or modification of life-expectancy guided palliative care until the patient's death or survivorship.

Special Palliative Care Interventions

Requests for Hastened Death

Special palliative care interventions include responses to requests for hastened death (ie, physician-assisted suicide or active euthanasia). The most appropriate response to a request for assisted suicide is to intensify palliative care. All such patients should be referred to a palliative care specialist. A request for hastened death often has important meanings that require exploration. Clarifying these meanings can sometimes enlarge the range of useful therapeutic options instead of providing a lethal prescription. Open exploration of the patient's request for aid in dying can often identify unmet needs and new palliative care interventions that may be helpful. Alternatives to physician-assisted suicide, such as withdrawal of life-sustaining treatment, voluntary cessation of eating and drinking, and/or sedation, should be considered and discussed with patients and families. Psychiatric consultation to diagnose and treat reversible causes of psychological suffering should be requested. Patients should be assured that their health care team is committed to providing continuing care. Although physician-assisted suicide, under specified conditions, is legal in the states of Oregon, Montana, and Washington, euthanasia is not legal in any of the United States. It is important for physicians to know the local legal status of hastened death, as other states have pending legislation regarding either prohibiting or permitting physician-assisted suicide.

Palliative Sedation

Palliative sedation can be an effective symptom-control treatment for imminently dying patients with refractory symptoms and a life expectancy of hours to days. Informed consent must be obtained from the patient and/or a surrogate or family member following discussions that clarify patient's disease status, treatment goals, prognosis, and expected outcomes. Clinicians may find that applying usual benefit/risk analysis to this type of intervention will suffice in medical decision-making. Palliative sedation has its ethical justification in the Doctrine of Double Effect,[149-154] which means that the possible harm (possible respiratory depression, starvation, and hastened death) that may come as a side-effect of doing good (relieving intolerable suffering) is justified. Furthermore, results from a recent study that prospectively matched terminally ill cancer patients receiving or not receiving palliative sedation suggest that sedation does not, in fact, shorten life.[155] An ethics consult may be considered in accordance with institutional guidelines and state regulations.

Palliative sedation is best performed by palliative care experts. The most common sedatives used for palliative sedation are thiopental, pentobarbital, and midazolam by parenteral infusions.[152] Infusional lorazepam, amobarbital, and propofol may also be used.[152, 156]

Care of the Imminently Dying Patient

An imminently dying patient is defined as one within hours of death who is not stable enough for transport. Care of the imminently dying patient is intense for the patient, family, and health care team. An end-of-life care order set that includes physical, practical, and psychosocial interventions may be beneficial for practitioners to use for imminently dying patients.

The physical aspects of care for an imminently dying patient focus on adequate symptom management and comfort, keeping in mind the patient's wishes and values. This may include intensifying ongoing care; adjusting medication doses for optimal comfort; discontinuing unnecessary interventions (diagnostic tests, transfusions, artificial nutrition, hydration, dialysis, needle sticks, etc.); ensuring access to symptom-relief medication through alternate routes if oral is difficult;

providing physical comfort by providing a pressure-relieving mattress and regular repositioning; treating urinary retention and fecal impaction; deactivation of implanted defibrillator; controlling terminal restlessness and agitation with palliative sedation; reducing death rattle/terminal secretion (repositioning patient, reducing parenteral and enteral fluids, adding medications such as scopolamine, hyoscyamine, atropine, or glycopyrrolate)[69]; and preparing for patient and family requests for autopsy and/or organ donation.

The psychosocial aspects of care for an imminently dying patient take into account individual and family goals, preferences, cultures, and religious beliefs. The care plan may include consultation with social workers or chaplains to meet identified social and spiritual needs; open communication between the patient, family, and care team regarding the physical and psychological aspects of the dying process and the importance of honoring any advance directives; and anticipatory grief counseling to help facilitate caregiver closure. Patients who are actively dying in their final hours of life should be allowed to spend uninterrupted time with family.

The practical aspects of care for an imminently dying patient in the hospital include mobilizing in-hospital end-of-life care policy and procedures, ensuring that the patient's advance directive is documented and implemented and a do-not-resuscitate order is written and followed, securing a private room for the patient, and enabling family presence around-the-clock. If the patient and family have not documented a do-not-resuscitate order, patient/family education and counseling should be intensified to try to help them accept this level of care to prevent harm to the patient from futile attempts at cardiopulmonary resuscitation. Dying patients and their families must be given respectful space and uninterrupted time together.

A Peaceful Death

These NCCN guidelines are the first to include death as an expected outcome and after-death care for the family as an essential part of the continuum of cancer care. Many studies have attempted to define a "good death" or a "peaceful death" from the perspective of clinicians, patients, and families.[157-160] Interestingly, one study found that patients, families, and physicians had very similar ideas of what constitutes a peaceful death: freedom from pain, being at spiritual peace, and being with family ranking among the top three considerations by all three groups.[160] End-of-life care should be flexible enough to ensure that the death is viewed as a peaceful death by those involved.[160] The definition of a "peaceful death" used by the NCCN Palliative Care panel is "one that is free from avoidable distress and suffering for patients, families and caregivers; in general accord with patient's and family's wishes; and consistent with clinical, cultural, and ethical standards."[22]

After-Death Care Interventions

Comprehensive palliative care for the patient's family and caregivers continues after the patient's death. Immediate issues include ensuring culturally sensitive and respectful treatment of the body, including removal of tubes, drains, lines, and the Foley catheter (unless an autopsy is planned); providing family time with the body; addressing survivor concerns about organ donation or autopsy; facilitating funeral arrangements through completion of necessary paperwork; and informing insurance companies and other health care providers of the patient's death. Bereavement support should be offered, beginning with a personal visit or telephone call from the patient's primary oncology team, followed by a condolence letter. Family members at risk for complicated bereavement or prolonged grief disorder should be identified, and complicated grief should be treated.[161-163] Bereavement care is often best provided by an experienced hospice team or a skilled mental health care professional. The family may request a debriefing

meeting from the medical team and may require assistance in identifying community bereavement resources. A well supported end-of-life care experience will facilitate the family's acceptance of appropriate referrals for cancer risk assessment and risk modification.

Psychosocial support should also be provided for the staff. A bereavement or memorial ritual for medical staff (eg, brief reading, moment of quiet) can be considered. Funeral attendance by health care professionals can be considered for individual patients. Health care professionals should also review medical issues related to patient death, explore concerns and questions about quality of patient care, and review emotional responses of family and staff to the patient's death. An emerging literature shows that health care professionals can be at risk for complicated bereavement, moral distress, or compassion fatigue[164-167]; such staff should be identified and assisted.

Putting Palliative Care Guidelines into Practice

These guidelines have the goal of providing the best quality of life possible for each patient and were developed to accompany the appropriate cancer treatment guidelines. 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. Patients and families 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. Skilled palliative care specialists and interdisciplinary palliative care teams, including board-certified palliative care physicians, advanced practice nurses, and physician assistants, should be readily available to provide consultative or direct care to patients and families who request or require the expertise. Finally, the quality of palliative care should be monitored by institutional quality improvement programs.

The experiences of patients with cancer throughout the disease course begin with the diagnosis. Patient conditions usually move from ambulatory to sedentary as disease advances and performance status worsens. When life expectancy is a matter of days or hours, patients may become unable to communicate. These patients may be at home, living with a family member, or in a health care facility. Through understanding the patient's status relative to the natural disease trajectory and by using these guidelines, the oncology team can provide the most appropriate treatment for each patient. Oncologists and patients should discuss at the outset whether the treatment will be curative or palliative. Many palliative care questions must be considered early in each patient's comprehensive cancer care. The primary oncology team is responsible for working with patients to raise and answer these questions. Oncologists must identify patients' goals for the remainder of life to get a better sense of whether they understood and accepted the diagnosis and prognosis. Additionally, oncologists must explain the types of therapies that are available and how these therapies can affect the patient's daily life. As the cancer progresses and the value of further anticancer therapy diminishes, palliative therapy should be intensified. The issue of whether patients want more anticancer therapy must be openly addressed. The delivery of clear and consistent prognostic information can help patients make the most appropriate decisions.

Patients should be made aware that undergoing anticancer therapy does not have to sidetrack them from addressing end-of-life issues. Collaborating with palliative care experts extends oncologists' therapeutic repertoire and diminishes the stress of caring for patients who have incurable disease. Increasing emphasis on palliative care in

oncology should improve patient outcomes and provide new avenues for clinical research and professional satisfaction. Timely introduction of members of the institutional or community palliative care team allows patients to meet the individuals who will help them and their families through their experience. Because the diagnosis of cancer and impending death is such a frightening experience, oncologists must try to alleviate those fears by assuring patients that the members of a team will work with them and their families to make things less burdensome. Additionally, oncologists must discuss the natural history of the patient's disease and prognosis with the family and palliative care team to anticipate and manage symptoms and problems commonly associated with the diagnosis and treatment of cancer.

Palliative care is intensified late in the course of disease to help patients and families understand the disease and begin to make end-of-life plans. Sometimes patients and families do not accept the prognosis or do not begin to make preparations.[168, 169] These things may be a sign that patients do not fully understand the disease and may lead to the desire by patients and families for aggressive treatments that may be both futile and toxic.[169] Palliative care supports education so that patients can better understand the disease.

Oncologists must ensure that advance care plans are in place as early as possible in the disease trajectory. This focus on the patients' wishes assures patients that they will be provided with no more and no less aggressive care than they desire and also relieves them of concerns about burdening family members with difficult end-of-life decisions. The combined efforts of the oncology team and the hospice/palliative care team can improve the overall outcome for patients and their families.

Hope

These guidelines are intended to help oncology teams provide the best care possible for patients with incurable cancer. The care outlined in these guidelines provides a different kind of hope than that for cure of the disease itself. Palliative care provides hope for dignity, comfort, and closure and for growth at the end of life.

Table 1

Palliative Care Internet Resources for Clinicians[a]

Palliative Care Clinical Competencies

www.epec.net
Education in Palliative and End-of-life Care (EPEC): Comprehensive curriculum covering fundamentals of palliative medicine; teaching guides

www.eperc.mcw.edu
End of Life / Palliative Education Resource Center (EPERC): Medical educator resources for peer-reviewed palliative care teaching materials

www.StopPain.org
Department of Pain Medicine and Palliative Care at Beth Israel Medical Center: Online education for physicians, nurses, and pharmacists

Clinical, educational, professional, and public resources

www.palliativedrugs.com
Palliativedrugs.com: Extensive information on pharmacologic symptom management

www.aahpm.org
American Academy of Hospice and Palliative Medicine: Physician membership organization; board review courses; publications

http://www.abim.org
The American Board of Internal Medicine: Physician Board Certification

http://www.nhpco.org/templates/1/homepage.cfm
National Hospice and Palliative Care Organization: Nonprofit membership organization representing hospice and palliative care programs and professionals in the United States.

http://www.hpna.org/
Hospice and Palliative Nurses Association: Specialty nursing organization with evidence-based educational tools for the nursing team

www.hms.harvard.edu/cdi/pallcare
Center for Palliative Care at Harvard Medical School: Faculty development courses, other educational programs

http://www.nationalconsensusproject.org/
National Consensus Project for Quality Palliative Care: Clinical practice guidelines

www.americangeriatrics.org/
American Geriatrics Society: Clinical guidelines and continuing education

Palliative Care Program Development

www.capc.org
Center to Advance Palliative Care: Technical assistance for clinicians and hospitals seeking to establish or strengthen a palliative care program

www.capc.org/pclc
Palliative Care Leadership Centers: Eight exemplary palliative care programs providing site visits, hands-on training, and technical assistance to support new palliative care clinicians and programs nationwide

[a] All websites accessed March, 2012.

Reprinted with permission from Khatcheressian J et al. Oncology 2005;19:1365-1376.

References

1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. CA Cancer J Clin 2012;62:10-29. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22237781.

2. Ferris FD, Bruera E, Cherny N, et al. Palliative cancer care a decade later: accomplishments, the need, next steps -- from the American Society of Clinical Oncology. J Clin Oncol 2009;27:3052-3058. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19451437.

3. Becker G, Hatami I, Xander C, et al. Palliative cancer care: an epidemiologic study. J Clin Oncol 2011;29:646-650. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21263094.

4. Seow H, Barbera L, Sutradhar R, et al. Trajectory of Performance Status and Symptom Scores for Patients With Cancer During the Last Six Months of Life. J Clin Oncol 2011. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21300920.

5. Berger A, Portenoy R, Weissman D, eds. Practice and Principles of Supportive Oncology. Philadelphia: Lippincott-Raven; 1998.

6. Doyle D, Hanks G, MacDonald Ne, eds. Oxford Textbook of Palliative Medicine. Oxford: Oxford University; 1998.

7. Emanuel L, von Gunten C, FD F, eds. The Education for Physicians on End-of-Life Care (EPEC) Curriculum. Princeton: The Robert Wood Johnson Foundation; 1999.

8. Peppercorn JM, Smith TJ, Helft PR, et al. American society of clinical oncology statement: toward individualized care for patients with advanced cancer. J Clin Oncol 2011;29:755-760. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21263086.

9. Smith TJ, Schnipper LJ. The American Society of Clinical Oncology program to improve end-of-life care. J Palliat Med 1998;1:221-230. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15859832.

10. Cancer pain relief and palliative care. Report of a WHO Expert Committee. World Health Organ Tech Rep Ser 1990;804:1-75. Available at: http://www.ncbi.nlm.nih.gov/pubmed/1702248.

11. Levy MH. Living with cancer: hospice/palliative care. J Natl Cancer Inst 1993;85:1283-1287. Available at: http://www.ncbi.nlm.nih.gov/pubmed/7688053.

12. Levy MH. Supportive oncology: forward. Semin Oncol 1994;21:699-700. Available at: http://www.ncbi.nlm.nih.gov/pubmed/7527594.

13. MacDonald N. Palliative care--the fourth phase of cancer prevention. Cancer Detect Prev 1991;15:253-255. Available at: http://www.ncbi.nlm.nih.gov/pubmed/1711926.

14. Elsayem A, Swint K, Fisch MJ, et al. Palliative Care Inpatient Service in a Comprehensive Cancer Center: Clinical and Financial Outcomes. J Clin Oncol 2004;22:2008-2014. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15143094.

15. Bergman J, Saigal CS, Lorenz KA, et al. Hospice use and high-intensity care in men dying of prostate cancer. Arch Intern Med 2011;171:204-210. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20937914.

16. NHPCO Facts and Figures: Hospice Care in America. National Hospice and Palliative Care Organization; 2011. Available at: http://www.nhpco.org/files/public/Statistics_Research/2011_Facts_Figures.pdf. Accessed March 2, 2012.

17. Earle CC, Neville BA, Landrum MB, et al. Trends in the Aggressiveness of Cancer Care Near the End of Life. J Clin Oncol 2004;22:315-321. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14722041.

18. Earle CC, Landrum MB, Souza JM, et al. Aggressiveness of cancer care near the end of life: is it a quality-of-care issue? J Clin Oncol

2008;26:3860-3866. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18688053.

19. Foley K, Gelband H, eds. Improving palliative care for cancer. Washington, DC: National Academy Press; 2001.

20. A controlled trial to improve care for seriously ill hospitalized patients. The study to understand prognoses and preferences for outcomes and risks of treatments (SUPPORT). The SUPPORT Principal Investigators. JAMA 1995;274:1591-1598. Available at: http://www.ncbi.nlm.nih.gov/pubmed/7474243.

21. Davis M. Integrating palliative medicine into an oncology practice. American Journal of Hospice & Palliative Medicine 2005;22:447-456. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16323715.

22. Field M, Cassel Ce, eds. Approaching Death: Improving Care at the End of Life. Washington, D.C: National Academy Press; 1997.

23. Malin JL. Bridging the divide: integrating cancer-directed therapy and palliative care. J Clin Oncol 2004;22:3438-3440. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15277538.

24. Meyers FJ, Linder J. Simultaneous care: disease treatment and palliative care throughout illness. J Clin Oncol 2003;21:1412-1415. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12663735.

25. Levy M. NCCN Task Force reports: Supportive and Palliative Care. Oncology 1999;13:517-522. Available at:

26. Weissman DE. Decision making at a time of crisis near the end of life. JAMA 2004;292:1738-1743. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15479939.

27. Chochinov HM. Dying, dignity, and new horizons in palliative end-of-life care. CA Cancer J Clin 2006;56:84-103; quiz 104-105. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16514136.

28. Kim A, Fall P, Wang D. Palliative care: optimizing quality of life. J Am Osteopath Assoc 2005;105:S9-14. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16368908.

29. de Haes H, Teunissen S. Communication in palliative care: a review of recent literature. Curr Opin Oncol 2005;17:345-350. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15933465.

30. Sinclair CT. Communicating a prognosis in advanced cancer. J Support Oncol 2006;4:201-204. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16669464.

31. Smith TJ, Temin S, Alesi ER, et al. American Society of Clinical Oncology Provisional Clinical Opinion: The Integration of Palliative Care into Standard Oncology Care. J Clin Oncol 2012. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22312101.

32. Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. N Engl J Med 2010;363:733-742. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20818875.

33. Greer JA, Pirl WF, Jackson VA, et al. Effect of Early Palliative Care on Chemotherapy Use and End-of-Life Care in Patients With Metastatic Non-Small-Cell Lung Cancer. J Clin Oncol 2012;30:394-400. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22203758.

34. Temel JS, Greer JA, Admane S, et al. Longitudinal perceptions of prognosis and goals of therapy in patients with metastatic non-small-cell lung cancer: results of a randomized study of early palliative care. J Clin Oncol 2011;29:2319-2326. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21555700.

35. Goelz T, Wuensch A, Stubenrauch S, et al. Specific training program improves oncologists' palliative care communication skills in a randomized controlled trial. J Clin Oncol 2011;29:3402-3407. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21825268.

36. Buss MK, Lessen DS, Sullivan AM, et al. Hematology/oncology fellows' training in palliative care: Results of a national survey. Cancer 2011;117:4304-4311. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21365618.

37. Lorenz KA, Lynn J, Dy SM, et al. Evidence for improving palliative care at the end of life: a systematic review. Ann Intern Med 2008;148:147-159. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18195339.

38. National Consensus Project for Quality Palliative Care. Clinical Practice Guidelines for Quality Palliative Care, Second Edition. 2009. Available at: http://www.nationalconsensusproject.org.

39. National Quality Forum: A National Framework and Preferred Practices for Palliative and Hospice Care Quality. 2006. Available at: http://www.qualityforum.org/Projects/n-r/Palliative_and_Hospice_Care_Framework/Palliative__Hospice_Care__Framework_and_Practices.aspx.

40. Qaseem A, Snow V, Shekelle P, et al. Evidence-based interventions to improve the palliative care of pain, dyspnea, and depression at the end of life: a clinical practice guideline from the American College of Physicians. Ann Intern Med 2008;148:141-146. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18195338.

41. Cancer Program Standards 2012: Ensuring Patient-Centered Care. American College of Surgeons Commission on Cancer; 2012. Available at: http://www.facs.org/cancer/coc/cocprogramstandards2012.pdf. Accessed March 1, 2012.

42. Weeks JC, Cook EF, O'Day SJ, et al. Relationship between cancer patients' predictions of prognosis and their treatment preferences. JAMA 1998;279:1709-1714. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9624023.

43. Lo B, Ruston D, Kates LW, et al. Discussing religious and spiritual issues at the end of life: a practical guide for physicians. JAMA 2002;287:749-754. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11851542.

44. Freelove R, Walling AD. Pancreatic cancer: diagnosis and management. Am Fam Physician 2006;73:485-492. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16477897.

45. Guarneri V, Conte PF. The curability of breast cancer and the treatment of advanced disease. Eur J Nucl Med Mol Imaging 2004;31 Suppl 1:S149-161. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15107948.

46. Pienta KJ, Smith DC. Advances in prostate cancer chemotherapy: a new era begins. CA Cancer J Clin 2005;55:300-318; quiz 323-305. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16166075.

47. Prommer E. Guidelines for the Use of Palliative Chemotherapy. AAHPM Bulletin 2004;5:2-13. Available at: http://www.aahpm.org/pdf/04spring.pdf.

48. Ajani JA. Evolving chemotherapy for advanced gastric cancer. Oncologist 2005;10 Suppl 3:49-58. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16368871.

49. Brown J, Thorpe H, Napp V, et al. Assessment of quality of life in the supportive care setting of the big lung trial in non-small-cell lung cancer. J Clin Oncol 2005;23:7417-7427. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16157935.

50. Silvestri GA, Rivera MP. Targeted therapy for the treatment of advanced non-small cell lung cancer: a review of the epidermal growth factor receptor antagonists. Chest 2005;128:3975-3984. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16354869.

51. Higginson IJ, Finlay IG, Goodwin DM, et al. Is there evidence that palliative care teams alter end-of-life experiences of patients and their caregivers? J Pain Symptom Manage 2003;25:150-168. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12590031.

52. Kinzbrunner BM. Hospice: what to do when anti-cancer therapy is no longer appropriate, effective, or desired. Semin Oncol 1994;21:792-798. Available at: http://www.ncbi.nlm.nih.gov/pubmed/7527597.

53. Ferrell B, Levy MH, Paice J. Managing pain from advanced cancer in the palliative care setting. Clin J Oncol Nurs 2008;12:575-581. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18676325.

54. Temel JS, Pirl WF, Lynch TJ. Comprehensive symptom management in patients with advanced-stage non-small-cell lung cancer. Clin Lung Cancer 2006;7:241-249. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16512977.

55. Dyspnea. Mechanisms, assessment, and management: a consensus statement. American Thoracic Society. Am J Respir Crit Care Med 1999;159:321-340. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9872857.

56. DeCamp MM, Jr., Mentzer SJ, Swanson SJ, Sugarbaker DJ. Malignant effusive disease of the pleura and pericardium. Chest 1997;112:291S-295S. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9337306.

57. Dy SM, Lorenz KA, Naeim A, et al. Evidence-based recommendations for cancer fatigue, anorexia, depression, and dyspnea. J Clin Oncol 2008;26:3886-3895. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18688057.

58. Swanson N, Mirza I, Wijesinghe N, Devlin G. Primary percutaneous balloon pericardiotomy for malignant pericardial effusion. Catheter Cardiovasc Interv 2008;71:504-507. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18307242.

59. Xue D, Abernethy AP. Management of dyspnea in advanced lung cancer: recent data and emerging concepts. Curr Opin Support Palliat Care 2010;4:85-91. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20440205.

60. Dy SM, Apostol CC. Evidence-based approaches to other symptoms in advanced cancer. Cancer J 2010;16:507-513. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20890148.

61. Ben-Aharon I, Gafter-Gvili A, Paul M, et al. Interventions for alleviating cancer-related dyspnea: a systematic review. J Clin Oncol 2008;26:2396-2404. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18467732.

62. Clemens KE, Quednau I, Klaschik E. Is there a higher risk of respiratory depression in opioid-naive palliative care patients during symptomatic therapy of dyspnea with strong opioids? J Palliat Med 2008;11:204-216. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18333735.

63. Jennings AL, Davies AN, Higgins JP, et al. A systematic review of the use of opioids in the management of dyspnoea. Thorax 2002;57:939-944. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12403875.

64. Simon ST, Higginson IJ, Booth S, et al. Benzodiazepines for the relief of breathlessness in advanced malignant and non-malignant diseases in adults. Cochrane Database Syst Rev 2010:CD007354. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20091630.

65. Back IN, Jenkins K, Blower A, Beckhelling J. A study comparing hyoscine hydrobromide and glycopyrrolate in the treatment of death rattle. Palliat Med 2001;15:329-336. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12054150.

66. Davis MP, Furste A. Glycopyrrolate: a useful drug in the palliation of mechanical bowel obstruction. J Pain Symptom Manage 1999;18:153-154. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10517034.

67. Hughes A, Wilcock A, Corcoran R, et al. Audit of three antimuscarinic drugs for managing retained secretions. Palliat Med 2000;14:221-222. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10858832.

68. Wildiers H, Menten J. Death rattle: prevalence, prevention and treatment. J Pain Symptom Manage 2002;23:310-317. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11997200.

69. Wildiers H, Dhaenekint C, Demeulenaere P, et al. Atropine, hyoscine butylbromide, or scopolamine are equally effective for the treatment of death rattle in terminal care. J Pain Symptom Manage 2009;38:124-133. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19361952.

70. Mirakhur RK, Dundee JW. Glycopyrrolate: pharmacology and clinical use. Anaesthesia 1983;38:1195-1204. Available at: http://www.ncbi.nlm.nih.gov/pubmed/6660460.

71. Grum DF, Osborne LR. Central anticholinergic syndrome following glycopyrrolate. Anesthesiology 1991;74:191-193. Available at: http://www.ncbi.nlm.nih.gov/pubmed/1986648.

72. Wingard DW. Glycopyrrolate and the central anticholinergic syndrome. Anesthesiology 1991;75:1125-1126. Available at: http://www.ncbi.nlm.nih.gov/pubmed/1741510.

73. #109 Death Rattle and Oral Secretions, 2nd ed. End of Life / Palliative Education Resource Center (EPERC); Available at: http://www.eperc.mcw.edu/fastFact/ff_109.htm. Accessed April 20, 2012.

74. Jensen D, Alsuhail A, Viola R, et al. Inhaled Fentanyl Citrate Improves Exercise Endurance During High-Intensity Constant Work Rate Cycle Exercise in Chronic Obstructive Pulmonary Disease. J Pain Symptom Manage 2011. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22168961.

75. Galbraith S, Fagan P, Perkins P, et al. Does the use of a handheld fan improve chronic dyspnea? A randomized, controlled, crossover trial. J Pain Symptom Manage 2010;39:831-838. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20471544.

76. Kumar NB, Kazi A, Smith T, et al. Cancer cachexia: traditional therapies and novel molecular mechanism-based approaches to treatment. Curr Treat Options Oncol 2010;11:107-117. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21128029.

77. Laviano A, Meguid MM, Inui A, et al. Therapy insight: Cancer anorexia-cachexia syndrome--when all you can eat is yourself. Nat Clin Pract Oncol 2005;2:158-165. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16264909.

78. Berenstein EG, Ortiz Z. Megestrol acetate for the treatment of anorexia-cachexia syndrome. Cochrane Database Syst Rev 2005:CD004310. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15846706.

79. Pascual Lopez A, Roque i Figuls M, Urrutia Cuchi G, et al. Systematic review of megestrol acetate in the treatment of anorexia-cachexia syndrome. J Pain Symptom Manage 2004;27:360-369. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15050664.

80. Yavuzsen T, Davis MP, Walsh D, et al. Systematic review of the treatment of cancer-associated anorexia and weight loss. J Clin Oncol 2005;23:8500-8511. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16293879.

81. Isenring EA, Capra S, Bauer JD. Nutrition intervention is beneficial in oncology outpatients receiving radiotherapy to the gastrointestinal or head and neck area. Br J Cancer 2004;91:447-452. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15226773.

82. Ravasco P, Monteiro-Grillo I, Vidal PM, Camilo ME. Dietary counseling improves patient outcomes: a prospective, randomized, controlled trial in colorectal cancer patients undergoing radiotherapy. J Clin Oncol 2005;23:1431-1438. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15684319.

83. Trentham K. Palliative Care. In: Marian M, Roberts S, eds. Clinical Nutrition for Oncology Patients. Sudbury, MA: Jones and Bartlett Publishers LLC; 2010.

84. Baldwin C, Spiro A, McGough C, et al. Simple nutritional intervention in patients with advanced cancers of the gastrointestinal tract, non-small cell lung cancers or mesothelioma and weight loss receiving chemotherapy: a randomised controlled trial. J Hum Nutr Diet 2011;24:431-440. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21733143.

85. August DA, Huhmann MB. A.S.P.E.N. clinical guidelines: nutrition support therapy during adult anticancer treatment and in hematopoietic cell transplantation. JPEN J Parenter Enteral Nutr 2009;33:472-500. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19713551.

86. McCann RM, Hall WJ, Groth-Juncker A. Comfort care for terminally ill patients. The appropriate use of nutrition and hydration. JAMA 1994;272:1263-1266. Available at: http://www.ncbi.nlm.nih.gov/pubmed/7523740.

87. Weiner RS, Kramer BS, Clamon GH, et al. Effects of intravenous hyperalimentation during treatment in patients with small-cell lung cancer. J Clin Oncol 1985;3:949-957. Available at: http://www.ncbi.nlm.nih.gov/pubmed/2991475.

88. Winter SM. Terminal nutrition: framing the debate for the withdrawal of nutritional support in terminally ill patients. Am J Med 2000;109:723-726. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11137488.

89. Schwartzberg L. Chemotherapy-induced nausea and vomiting: state of the art in 2006. J Support Oncol 2006;4:3-8. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16499138.

90. Shoemaker LK, Estfan B, Induru R, Walsh TD. Symptom management: an important part of cancer care. Cleve Clin J Med 2011;78:25-34. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21199904.

91. Holt DW, Volans GN. Gastrointestinal symptoms of digoxin toxicity. Br Med J 1977;2:704. Available at: http://www.ncbi.nlm.nih.gov/pubmed/268993.

92. Hwang WJ, Tsai JJ. Acute phenytoin intoxication: causes, symptoms, misdiagnoses, and outcomes. Kaohsiung J Med Sci 2004;20:580-585. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15696787.

93. Buzdar AU, Esparza L, Natale R, et al. Lorazepam-enhancement of the antiemetic efficacy of dexamethasone and promethazine. A placebo-controlled study. Am J Clin Oncol 1994;17:417-421. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8092114.

94. Tan L, Liu J, Liu X, et al. Clinical research of Olanzapine for prevention of chemotherapy-induced nausea and vomiting. J Exp Clin Cancer Res 2009;28:131. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19775450.

95. Hardy JR, O'Shea A, White C, et al. The efficacy of haloperidol in the management of nausea and vomiting in patients with cancer. J Pain Symptom Manage 2010;40:111-116. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20619214.

96. Gralla RJ, Itri LM, Pisko SE, et al. Antiemetic efficacy of high-dose metoclopramide: randomized trials with placebo and prochlorperazine in patients with chemotherapy-induced nausea and vomiting. N Engl J Med 1981;305:905-909. Available at: http://www.ncbi.nlm.nih.gov/pubmed/7024807.

97. Grunberg SM, Stevenson LL, Russell CA, McDermed JE. Dose ranging phase I study of the serotonin antagonist GR38032F for prevention of cisplatin-induced nausea and vomiting. J Clin Oncol 1989;7:1137-1141. Available at: http://www.ncbi.nlm.nih.gov/pubmed/2526864.

98. Marty M, Pouillart P, Scholl S, et al. Comparison of the 5-hydroxytryptamine3 (serotonin) antagonist ondansetron (GR 38032F)

with high-dose metoclopramide in the control of cisplatin-induced emesis. N Engl J Med 1990;322:816-821. Available at: http://www.ncbi.nlm.nih.gov/pubmed/2137902.

99. Kris MG, Gralla RJ, Clark RA, et al. Antiemetic control and prevention of side effects of anti-cancer therapy with lorazepam or diphenhydramine when used in combination with metoclopramide plus dexamethasone. A double-blind, randomized trial. Cancer 1987;60:2816-2822. Available at: http://www.ncbi.nlm.nih.gov/pubmed/3315176.

100. Aapro MS, Plezia PM, Alberts DS, et al. Double-blind crossover study of the antiemetic efficacy of high-dose dexamethasone versus high-dose metoclopramide. J Clin Oncol 1984;2:466-471. Available at: http://www.ncbi.nlm.nih.gov/pubmed/6539363.

101. Navari RM, Einhorn LH, Passik SD, et al. A phase II trial of olanzapine for the prevention of chemotherapy-induced nausea and vomiting: a Hoosier Oncology Group study. Support Care Cancer 2005;13:529-534. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15700131.

102. Herman TS, Einhorn LH, Jones SE, et al. Superiority of nabilone over prochlorperazine as an antiemetic in patients receiving cancer chemotherapy. N Engl J Med 1979;300:1295-1297. Available at: http://www.ncbi.nlm.nih.gov/pubmed/375088.

103. Morita T, Takigawa C, Onishi H, et al. Opioid rotation from morphine to fentanyl in delirious cancer patients: an open-label trial. J Pain Symptom Manage 2005;30:96-103. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16043013.

104. Mamtani R, Cimino A. A primer of complementary and alternative medicine and its relevance in the treatment of mental health problems. Psychiatr Q 2002;73:367-381. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12418362.

105. Mansky PJ, Wallerstedt DB. Complementary medicine in palliative care and cancer symptom management. Cancer J 2006;12:425-431. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17034678.

106. Marchioro G, Azzarello G, Viviani F, et al. Hypnosis in the treatment of anticipatory nausea and vomiting in patients receiving cancer chemotherapy. Oncology 2000;59:100-104. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10971166.

107. Davis MP, Hallerberg G. A systematic review of the treatment of nausea and/or vomiting in cancer unrelated to chemotherapy or radiation. J Pain Symptom Manage 2010;39:756-767. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20413062.

108. Becker G, Galandi D, Blum HE. Peripherally acting opioid antagonists in the treatment of opiate-related constipation: a systematic review. J Pain Symptom Manage 2007;34:547-565. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17900855.

109. Mancini I, Bruera E. Constipation in advanced cancer patients. Support Care Cancer 1998;6:356-364. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9695203.

110. American Pain Socitey. Principles ofAnalgesic use in the treatment of acute pain and cancer pain (ed 5th). Glenview, IL: American Pain Society; 2003.

111. Hawley PH, Byeon JJ. A comparison of sennosides-based bowel protocols with and without docusate in hospitalized patients with cancer. J Palliat Med 2008;11:575-581. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18454610.

112. Portenoy RK, Thomas J, Moehl Boatwright ML, et al. Subcutaneous methylnaltrexone for the treatment of opioid-induced constipation in patients with advanced illness: a double-blind, randomized, parallel group, dose-ranging study. J Pain Symptom Manage 2008;35:458-468. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18440447.

113. Thomas J, Karver S, Cooney GA, et al. Methylnaltrexone for opioid-induced constipation in advanced illness. N Engl J Med 2008;358:2332-2343. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18509120.

114. Mercadante S, Casuccio A, Mangione S. Medical treatment for inoperable malignant bowel obstruction: a qualitative systematic review. J Pain Symptom Manage 2007;33:217-223. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17280927.

115. Porzio G, Aielli F, Verna L, et al. Can malignant bowel obstruction in advanced cancer patients be treated at home? Support Care Cancer 2011;19:431-433. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20872024.

116. Mercadante S, Ferrera P, Villari P, Marrazzo A. Aggressive pharmacological treatment for reversing malignant bowel obstruction. J Pain Symptom Manage 2004;28:412-416. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15471659.

117. Baron TH. Interventional palliative strategies for malignant bowel obstruction. Curr Oncol Rep 2009;11:293-297. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19508834.

118. Brooksbank MA, Game PA, Ashby MA. Palliative venting gastrostomy in malignant intestinal obstruction. Palliat Med 2002;16:520-526. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12465700.

119. Palesh OG, Roscoe JA, Mustian KM, et al. Prevalence, demographics, and psychological associations of sleep disruption in patients with cancer: University of Rochester Cancer Center-Community Clinical Oncology Program. J Clin Oncol 2010;28:292-298. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19933917.

120. Savard J, Ivers H, Villa J, et al. Natural course of insomnia comorbid with cancer: an 18-month longitudinal study. J Clin Oncol 2011;29:3580-3586. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21825267.

121. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 1991;14:540-545. Available at: http://www.ncbi.nlm.nih.gov/pubmed/1798888.

122. Payne RJ, Hier MP, Kost KM, et al. High prevalence of obstructive sleep apnea among patients with head and neck cancer. J Otolaryngol 2005;34:304-311. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16181591.

123. Stern TP, Auckley D. Obstructive sleep apnea following treatment of head and neck cancer. Ear Nose Throat J 2007;86:101-103. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17385619.

124. Antonescu-Turcu A, Parthasarathy S. CPAP and bi-level PAP therapy: new and established roles. Respir Care 2010;55:1216-1229. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20800002.

125. Berger AM. Update on the state of the science: sleep-wake disturbances in adult patients with cancer. Oncol Nurs Forum 2009;36:E165-177. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19581220.

126. Harsora P, Kessmann J. Nonpharmacologic management of chronic insomnia. Am Fam Physician 2009;79:125-130. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19178064.

127. Jungquist CR, O'Brien C, Matteson-Rusby S, et al. The efficacy of cognitive-behavioral therapy for insomnia in patients with chronic pain. Sleep Med 2010;11:302-309. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20133188.

128. Kim SW, Shin IS, Kim JM, et al. Effectiveness of mirtazapine for nausea and insomnia in cancer patients with depression. Psychiatry Clin Neurosci 2008;62:75-83. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18289144.

129. Stewart SA. The effects of benzodiazepines on cognition. J Clin Psychiatry 2005;66 Suppl 2:9-13. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15762814.

130. Bruera E, Fainsinger R, MacEachern T, Hanson J. The use of methylphenidate in patients with incident cancer pain receiving regular opiates. A preliminary report. Pain 1992;50:75-77. Available at: http://www.ncbi.nlm.nih.gov/pubmed/1381072.

131. 2011 Physicians' Desk Reference (ed 65). Montvale, NJ: PDR Network, LLC; 2010.

132. Diagnostic and statistical manual of mental disorders (ed 4th). Washington, DC: American Psychiatric Association; 1994.

133. Devlin JW, Roberts RJ, Fong JJ, et al. Efficacy and safety of quetiapine in critically ill patients with delirium: a prospective, multicenter, randomized, double-blind, placebo-controlled pilot study. Crit Care Med 2010;38:419-427. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19915454.

134. Grover S, Mattoo SK, Gupta N. Usefulness of Atypical Antipsychotics and Choline Esterase Inhibitors in Delirium: A Review. Pharmacopsychiatry 2011. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21394715.

135. Maher AR, Maglione M, Bagley S, et al. Efficacy and comparative effectiveness of atypical antipsychotic medications for off-label uses in adults: a systematic review and meta-analysis. JAMA 2011;306:1359-1369. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21954480.

136. Lacasse H, Perreault MM, Williamson DR. Systematic review of antipsychotics for the treatment of hospital-associated delirium in medically or surgically ill patients. Ann Pharmacother 2006;40:1966-1973. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17047137.

137. Jacobson SA. Delirium in the elderly. Psychiatr Clin North Am 1997;20:91-110. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9139298.

138. Caraceni A, Nanni O, Maltoni M, et al. Impact of delirium on the short term prognosis of advanced cancer patients. Italian Multicenter Study Group on Palliative Care. Cancer 2000;89:1145-1149. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10964345.

139. Kehl KA. Treatment of terminal restlessness: a review of the evidence. J Pain Palliat Care Pharmacother 2004;18:5-30. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15148006.

140. Mack JW, Cronin A, Taback N, et al. End-of-Life Care Discussions Among Patients With Advanced Cancer: A Cohort Study. Ann Intern Med 2012;156:204-210. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22312140.

141. Wright AA, Keating NL, Balboni TA, et al. Place of death: correlations with quality of life of patients with cancer and predictors of bereaved caregivers' mental health. J Clin Oncol 2010;28:4457-4464. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20837950.

142. Han B, Remsburg RE, McAuley WJ, et al. National trends in adult hospice use: 1991-1992 to 1999-2000. Health Aff (Millwood) 2006;25:792-799. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16684745.

143. Elsayem A, Smith ML, Parmley L, et al. Impact of a palliative care service on in-hospital mortality in a comprehensive cancer center. J Palliat Med 2006;9:894-902. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16910804.

144. Khatcheressian J, Cassel JB, Lyckholm L, et al. Improving palliative and supportive care in cancer patients. Oncology (Williston Park) 2005;19:1365-1376; discussion 1377-1368, 1381-1362, 1384 passim. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16285228.

145. Levy MH. Supportive oncology-palliative care: what's in a name? Semin Oncol 2005;32:131-133. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15815956.

146. Morrison RS, Meier DE. Clinical practice. Palliative care. N Engl J Med 2004;350:2582-2590. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15201415.

147. Singer PA, Martin DK, Kelner M. Quality end-of-life care: patients' perspectives. JAMA 1999;281:163-168. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9917120.

148. Byock I, ed Dying Well: The Prospect for Growth at the End of Life. New York: Riverhead Books; 1997.

149. Braun TC, Hagen NA, Clark T. Development of a clinical practice guideline for palliative sedation. J Palliat Med 2003;6:345-350. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14509479.

150. Cherny NI, Portenoy RK. Sedation in the management of refractory symptoms: guidelines for evaluation and treatment. J Palliat Care 1994;10:31-38. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8089815.

151. Cowan JD, Palmer TW. Practical guide to palliative sedation. Curr Oncol Rep 2002;4:242-249. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11937015.

152. Levy MH, Cohen SD. Sedation for the relief of refractory symptoms in the imminently dying: a fine intentional line. Semin Oncol 2005;32:237-246. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15815971.

153. Sykes N, Thorns A. The use of opioids and sedatives at the end of life. Lancet Oncol 2003;4:312-318. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12732169.

154. Wein S. Sedation in the imminently dying patient. Oncology (Williston Park) 2000;14:585-592; discussion 592, 597-588, 601. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10826317.

155. Maltoni M, Pittureri C, Scarpi E, et al. Palliative sedation therapy does not hasten death: results from a prospective multicenter study. Ann Oncol 2009;20:1163-1169. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19542532.

156. Cherny NI, Radbruch L. European Association for Palliative Care (EAPC) recommended framework for the use of sedation in palliative care. Palliat Med 2009;23:581-593. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19858355.

157. Hughes T, Schumacher M, Jacobs-Lawson JM, Arnold S. Confronting death: perceptions of a good death in adults with lung cancer. Am J Hosp Palliat Care 2008;25:39-44. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18160544.

158. Kehl KA. Moving toward peace: an analysis of the concept of a good death. Am J Hosp Palliat Care 2006;23:277-286. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17060291.

159. Mak JM, Clinton M. Promoting a good death: an agenda for outcomes research--a review of the literature. Nurs Ethics 1999;6:97-106. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10358525.

160. Steinhauser KE, Christakis NA, Clipp EC, et al. Factors considered important at the end of life by patients, family, physicians, and other care providers. JAMA 2000;284:2476-2482. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11074777.

161. Guldin MB, Vedsted P, Zachariae R, et al. Complicated grief and need for professional support in family caregivers of cancer patients in palliative care: a longitudinal cohort study. Support Care Cancer 2011. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21892795.

162. Kacel E, Gao X, Prigerson HG. Understanding bereavement: what every oncology practitioner should know. J Support Oncol 2011;9:172-180. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22024306.

163. Zhang B, El-Jawahri A, Prigerson HG. Update on bereavement research: evidence-based guidelines for the diagnosis and treatment of complicated bereavement. J Palliat Med 2006;9:1188-1203. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17040157.

164. Cohen JS, Erickson JM. Ethical dilemmas and moral distress in oncology nursing practice. Clin J Oncol Nurs 2006;10:775-780. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17193943.

165. Gaeta S, Price KJ. End-of-life issues in critically ill cancer patients. Crit Care Clin 2010;26:219-227. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19944283.

166. Irvin S. The experiences of the registered nurse caring for the person dying of cancer in a nursing home. Collegian 2000;7:30-34. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11858309.

167. Najjar N, Davis LW, Beck-Coon K, Carney Doebbeling C. Compassion fatigue: a review of the research to date and relevance to cancer-care providers. J Health Psychol 2009;14:267-277. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19237494.

168. Hartmann LC. Unrealistic expectations. J Clin Oncol 2005;23:4231-4232; discussion 4233-4234. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15961772.

169. Kalemkerian GP. Commentary on "Unrealistic Expectations". J Clin Oncol 2005;23:4233-4234. Available at: http://jco.ascopubs.org/content/23/18/4233.short.