National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Palliative Care

Version 2.2019 — February 8, 2019

NCCN.org

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Discussion

***Maria Dans, MD/Chair £**
Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine

***Jean S. Kutner, MD/Vice-Chair ₪ Þ £**
University of Colorado Cancer Center

Justin N. Baker, MD €
St. Jude Children's Research Hospital/The University of Tennessee Health Science Center

Jessica R. Bauman, MD †
Fox Chase Cancer Center

Anna C. Beck, MD
Huntsman Cancer Institute at the University of Utah

Toby C. Campbell, MD † £
University of Wisconsin Carbone Cancer Center

Amy A. Case, MD £
Roswell Park Comprehensive Cancer Center

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

Danielle Doberman, MD £
The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

Howard Edwards, MD £
Fred & Pamela Buffett Cancer Center

Andrew S. Epstein, MD † £
Memorial Sloan Kettering Cancer Center

Thomas R. Fitch, MD £
Mayo Clinic Cancer Center

Jennifer Kapo, MD £
Yale Cancer Center/Smilow Cancer Hospital

Richard T. Lee, MD £ †
Case Comprehensive Cancer Center/University Hospitals Seidman Cancer Center and Cleveland Clinic Taussig Cancer Institute

Elizabeth T. Loggers, MD, PhD £ †
Fred Hutchinson Cancer Research Center/Seattle Cancer Care Alliance

Susan McCammon, MD Þ £
University of Alabama at Birmingham Comprehensive Cancer Center

Charles Miller, MD £
The Ohio State University Comprehensive Cancer Center - James Cancer Hospital and Solove Research Institute

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

William Mitchell, MD £ †
UC San Diego Moores Cancer Center

Diane G. Portman, MD £
Moffitt Cancer Center

David Spiegel, MD θ
Stanford Cancer Institute

Linda Sutton, MD † £
Duke Cancer Institute

Eytan Szmuilowicz, MD £
Robert H. Lurie Comprehensive Cancer Center of Northwestern University

Jennifer Temel, MD † £
Massachusetts General Hospital Cancer Center

Jane Thomas, MD £
Dana-Farber Cancer Institute

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

Finly Zachariah, MD £
City of Hope National Medical Center

NCCN
Mary Anne Bergman
Jillian Scavone, PhD

[NCCN Guidelines Panel Disclosures]

Continue

† Medical oncology
‡ Hematology/Hematology oncology
Þ Internal medicine
€ Pediatric oncology
£ Supportive care including palliative and pain management
θ Psychiatry and psychology, including health behavior
ψ Neurology/Neuro-oncology
φ Anesthesiology
₪ Geriatric medicine
* Discussion Section Writing Committee

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

To find clinical trials online at NCCN Member Institutions, click here: nccn.org/clinical_trials/clinicians.aspx.

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

See NCCN Categories of Evidence and Consensus.

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Discussion

Updates in Version 2.2019 of the NCCN Guidelines for Palliative Care from Version 1.2019 include:

MS-1

- **The Discussion section has been updated to reflect the changes in the algorithm**

Updates in Version 1.2019 of the NCCN Guidelines for Palliative Care from Version 1.2018 include:

PAL-1

Definition of Palliative Care

- **Modified: "Palliative care is an approach to patient/family/caregiver-centered health care that focuses on optimal management of ~~pain and other~~ distressing symptoms, while incorporating psychosocial and spiritual care according to patient/family/*caregiver* needs, values, beliefs, and cultures. The goal of palliative care is to anticipate, prevent, and reduce suffering and to support the best possible quality of life for patients/families/caregivers, regardless of the stage of the disease or the need for other therapies. Palliative care can begin 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 *provided* ~~initiated~~ by the primary oncology team and ~~then~~ augmented *as needed* by collaboration with an interdisciplinary team of palliative care experts."**

Standards of Palliative Care

- **Modified 5th bullet: "Palliative care specialists and interdisciplinary palliative care teams, including board-certified palliative care physicians, advanced practice nurses, physician assistants, social workers, chaplains, and pharmacists, should be readily available to provide consultative or direct care to patients/families/caregivers *and/or health care professionals* who request or require their expertise."**

PAL-2

Reassessment

- **Modified 2nd bullet: Adequate ~~pain and~~ symptom management (throughout the guidelines)**
- **Modified 5th bullet: *Decreased* ~~Relief of~~ caregiver burden (throughout the guidelines)**

PAL-2 continued

Footnotes

- **Footnote "d" modified: "Patients with one or more positive indicators *may benefit from* ~~require~~ a care plan developed by an interdisciplinary team of physicians, nurses, social workers, mental health professionals, chaplains, advanced practice clinicians and dietitians."**

PAL-3

Indications

- **Modified 7th bullet, 10th sub-bullet: "Palliative stenting or *need for* venting gastrostomy."**

PAL-6

If unacceptable

Modified 2nd bullet: "Consult with a mental health professional *and/or addiction specialist* to evaluate and treat undiagnosed psychiatric disorders, substance abuse, and inadequate coping methods"

PAL-8

Assessment/Complex patient/family/caregiver circumstances

- **4th bullet, "*Substance abuse*" is new to the page**

Assessment/Oncology care team/staff challenges

- **Modified 1st bullet: "Complex care coordination issues *within and* among multiple care teams"**
- **Modified 2nd bullet: "*Compromised* resilience including"**
- **Modified 3rd sub-bullet: "Burnout ~~training~~"**

PAL-9

Interventions

- **"Provide *primary palliative care, including anti-cancer treatment and disease-related care planning*" is a new bullet for years to months.**
- **Modified the last bullet for months to weeks as follows: "Offer ~~best~~ *goal-directed* supportive care, including referral to *specialized* palliative care *services* or hospice."**

PAL-11

Interventions

- **Pharmacologic therapy has been modified as follows:**
  - **~~Consider~~ Opioids**
  - ***Consider* benzodiazepines *if coexisting anxiety***

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Updates in Version 1.2019 of the NCCN Guidelines for Palliative Care from Version 1.2018 include:

PAL-11 continued

Footnotes

- ***"The addition of benzodiazepines to opioids can increase the risk of respiratory depression"*** **is a new footnote corresponding to "Consider benzodiazepines if coexisting anxiety."**

PAL-12

Interventions

- ***"Cooler temperatures"*** **was added to "fans" under nonpharmacologic therapies to relieve symptoms.**

PAL-13

If unacceptable

Deleted: "Consider clinical trial"

PAL-14

Interventions

- **1st sub-bullet is new to the page for months to weeks: "Consider psychiatric consultation if patient has an eating disorder"**
- **Deleted the following bullets: "Provide family/caregiver(s) with alternate ways of caring for the patient" and "Treat reversible causes"**

PAL-15

Nausea and Vomiting/Interventions

- **Medication/*Substance*-induced, 2nd sub-bullet added: "*Review use of marijuana/cannabis for possible cannabis-associated hyperemesis syndrome and counsel regarding cessation if indicated*."**

PAL-16

Persistent Nausea and Vomiting/Interventions

- ***This page has been significiantly modified***

PAL-17

Constipation

- **Preventive Measures, 2nd sub-bullet: "Increase ~~dose of laxative ± osmotic~~ laxative *dose* with goal of 1 non-forced bowel movement (BM) every 1–2 days"**
- **Constipation present, 6th bullet: "Add and titrate ~~bisacodyl~~ stimulant and/or osmotic laxative ~~with a goal of 1 non-forced BM every 1–2 days~~"**
- **The following references are new to "Constipation":**
  - **Wickham RJ. Managing constipation in adults with cancer. J Adv Pract Oncol 2017;8(2):149-161.**
  - **Larkin PJ, Cherny NI, LaCarpia D, et al. Diagnosis, assessment and management of constipation in advanced cancer: ESMO Clinical Practice Guidelines. Ann Oncol 2018;29 (Suppl 4):iv111-iv125.**

PAL-18

Diarrhea

- **Interventions, Further Assessment, 3rd bullet: "~~CAUSE~~ Tailor treatment to potential causes."**

PAL-19

Antidiarrheal Interventions

- **6th bullet: "GRADE 2:If chemotherapy-induced, *decrease or delay the next dose of chemotherapy"***

7th bullet, 4th sub-bullet: "See Management of Immunotherapy Related Toxicity Guidelines *for immunotherapy-related diarrhea"*

PAL-25

Social Support/Resource Management

- **Interventions, 1st bullet modified: "*Assess* ~~Consider~~"**
- **1st sub-bullet modified: *"Coping and adjustment to illness by patient/family/caregivers"***
- **6th sub-bullet: "~~Consider~~ *Culture-specific needs"***
- **2nd bullet: "*Obtain medical interpreters/translators as needed who are not related to the patient"* is new to the page.**
- ***4th bullet, 3rd sub-bullet: "Art and music therapy, if available"***

PAL-29

Advance Care Planning/Interventions

- **2nd bullet: "Assess decision-making capacity and ~~need for~~ identify surrogate decision-maker *if necessary"***
- **3rd bullet: "Explore fears about *the future and provide emotional support* ~~dying and address anxiety~~"**
- **4th bullet: "Initiate discussion of personal values and *care* preferences ~~for end-of-life care~~"**

If unacceptable

- **3rd bullet: "Refer to *specialized* palliative care *service* if the patient is having difficulty engaging in discussion of advance care planning"**
- **5th bullet: "Consider *referral to spiritual care counselor*"**

PAL-30

Interventions

- **Months to weeks, modified last bullet as follows: "Explore fears about *dying and address concerns* ~~*anxiety* the future and provide emotional support~~"**
- **Weeks to days (dying patient), modified last bullet as follows: "Encourage the patient/family/caregiver ~~to limit~~ *as appropriate to avoid* CPR with the use of do not resuscitate (DNR)/do not attempt resuscitation (DNAR)/allow natural death (AND) *orders"***

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Updates in Version 1.2019 of the NCCN Guidelines for Palliative Care from Version 1.2018 include:

PAL-31

Response to Requests for Hastened Death

- 10th bullet, 4th sentence: "Consider a consultation with an ethics committee, *specialized* palliative care service, or experienced colleague"

PAL-32

Care of the Imminently Dying Hospitalized Patient

Physical

- 11th sub-bullet: "*Treat delirium (See PAL-24)"*
- 12th sub-bullet: "*Consider* palliative sedation ~~treat~~ *for* refractory restlessness and agitation ~~with palliative sedation~~ (See PAL-33)"

Care of the Imminently Dying Hospitalized Patient

Psychosocial

- 3rd sub-bullet deleted: "Allow the patient/family/caregiver to have uninterrupted time together and encourage continued communication"

Practical

- 3rd sub-bullet: "Discuss and document patient/family/caregiver wishes for resuscitation. In the event that CPR is unlikely to be effective, recommend other options such as do not resuscitate (DNR)/ do not attempt resuscitation (DNAR)/ allow natural death (AND) orders and promote~~ing~~ comfort care."
- Sub-bullet deleted: "If the patient/family/caregiver have not documented a DNAR order, intensify patient/family/caregiver education, counsel on the importance of a DN~~A~~R or AND *order"*

PAL-33

Palliative Sedation

- Reordered the following bullets:
- *Palliative sedation to unconsciousness, in which the intended effect is deep sedation, remains controversial.*
- *Refractory symptoms are symptoms that cannot be adequately managed despite comprehensive, interdisciplinary palliative care that does not compromise consciousness.*
- Confirm that the patient has refractory symptoms and is imminently dying.
  - *Imminently dying patients have a prognosis of hours to days. If palliative sedation is being considered, prognosis should be confirmed by two physicians.*

PAL-33 continued

- 4th bullet, 4th sub-bullet modified:~~Explain that consent for palliative sedation in some cases requires must be accompanied by consent for:~~ Discontinuation of life-prolonging therapies (such as artificial hydration/nutrition *and/or* withholding of cardiopulmonary resuscitation) *often accompanies palliative* sedation.

PAL-A (1 of 5)

Secretions

- Modified: "Scopolamine, 0.4 mg SC q4h PRN/1.5 mg patches, 1–3 patches q *72 hours..."*
- *Route of administration has been clarified throughout the guidelines.*

PAL-A (2 of 5)

Nausea and Vomiting (NV)-Initial Treatment

- Modified: "Haloperidol, 0.5 mg PO TID OR metoclopramide, 5–10 mg PO QID 30 min before meals and at bedtime OR prochlorperazine, 5–10 mg PO 3–4 times/d, maximum 40 mg/d OR olanzapine, 5–10 mg PO 2–3 times/d OR ondansetron, *4 mg PO q4h or 8 mg PO q8h*"

Nausea and Vomiting (NV)-Initial Treatment

- Modified: "Prescribe oral, sublingual, or rectal agent and titrate to maximum benefit~~; consider opioid rotation~~"
- Modified: "If NV persists, provide ~~IV administration~~ PRN, scheduled, or continuous parenteral infusion as necessary"
- Deleted: "If NV persists, provide scheduled IV administration or continuous infusion"
- Added: "Consider subcutaneous administration as an alternative"

Constipation

- Modified: "Prophylaxis: *Titrate the* senna *and add polyethylene glycol, recommend starting with polyethylene glycol if the patient is not on opioids and can tolerate the volume of liquid"*

PAL-A (3 of 5)

Diarrhea

- Deleted: "Consider scopolamine, 0.4 mg SC every 4 h PRN"
- Added: "*Atropine 0.5–1 mg SC/IV/SL q 4–6h PRN*"

PAL-A (5 of 5)

Delirium

- Modified: "Upward titrate haloperidol, risperidone or olanzapine ~~or quetiapine fumarate"~~

Definition of Palliative Care[a,c]

Palliative care is an approach to patient/family/caregiver-centered health care that focuses on optimal management of distressing symptoms, while incorporating psychosocial and spiritual care according to patient/family/caregiver needs, values, beliefs, and cultures. The goal of palliative care is to anticipate, prevent, and reduce suffering and to support the best possible quality of life for patients/families/caregivers, regardless of the stage of the disease or the need for other therapies. Palliative care can begin 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 provided by the primary oncology team and augmented as needed by collaboration with an interdisciplinary team of palliative care experts.

Standards of Palliative Care[b,c]

- **Institutions should develop processes for integrating palliative care into cancer care, both as part of usual oncology care and for patients with specialty palliative care needs.**
- **All cancer patients should be screened for palliative care needs at their initial visit, at appropriate intervals, and as clinically indicated.**
- **Patients/families/caregivers should be informed that palliative care is an integral part of their comprehensive cancer care.**
- **Educational programs should be provided to all health care professionals and trainees so that they can develop effective palliative care knowledge, skills, and attitudes.**
- **Palliative care specialists and interdisciplinary palliative care teams, including board-certified palliative care physicians, advanced practice nurses, physician assistants, social workers, chaplains, and pharmacists, should be readily available to provide consultative or direct care to patients/families/caregivers and/or health care professionals who request or require their expertise.**
- **Quality of palliative care should be monitored by institutional quality improvement programs.**

[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.
[c]IOM (Institute of Medicine). 2014 Dying in America: Improving quality and honoring individual preferences near the end of life. Washington, DC: The National Academies Press. (www.nap.edu/read/18748/chapter/1)

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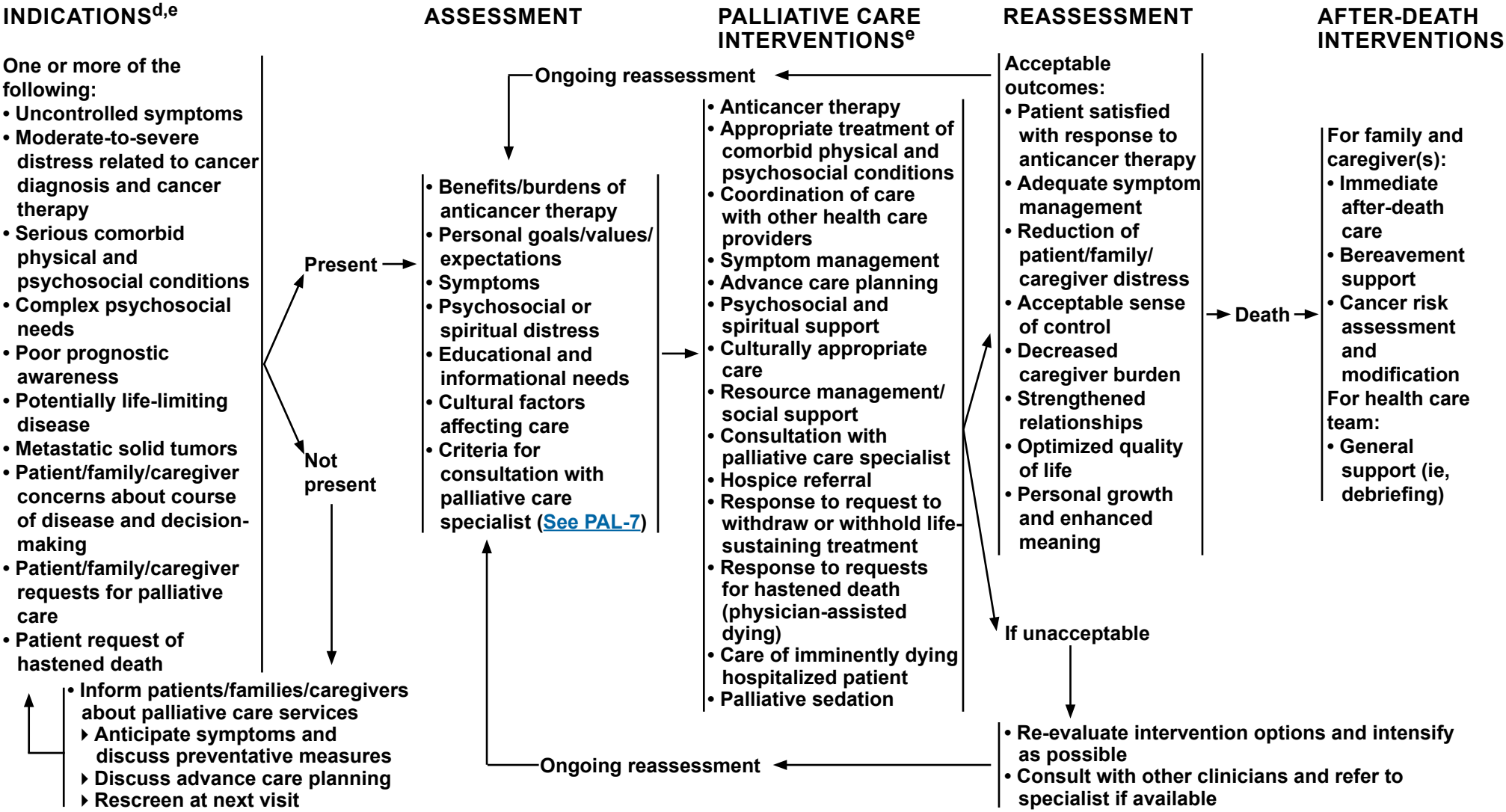

[d]Patients with one or more positive indicators may benefit from a care plan developed by an interdisciplinary team of physicians, nurses, social workers, mental health professionals, chaplains, advanced practice clinicians, and dietitians.

[e]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.

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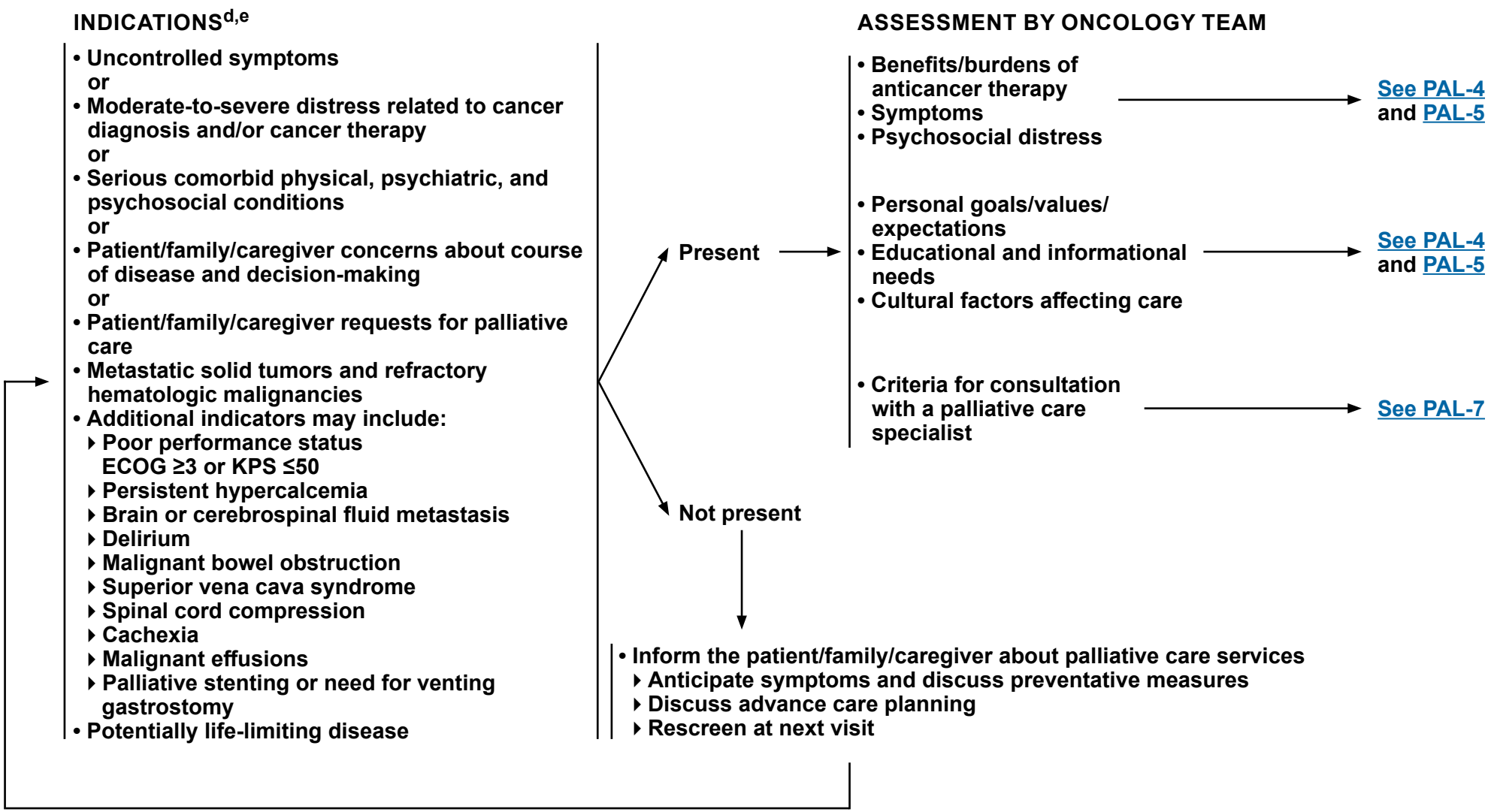
Assessment by Oncology Team (PAL-3)



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ASSESSMENT BY ONCOLOGY TEAM

Benefits/burdens of anticancer therapy →
- Natural history of specific tumor
- Potential for response to further treatment
- Potential for treatment-related toxicities
- Patient's understanding of disease prognosis
- Goals and meaning of anticancer therapy for patient/family/caregiver(s)
- Impairment of vital organs
- Performance status
- Serious comorbid conditions

→ Anticancer therapy interventions (See PAL-9)

Patient/family/caregiver(s) goals/values/ expectations/ priorities →
- Shared decision-making with patient/family/caregiver(s)
- Advance care planning
- Goals and meaning of anticancer therapy
- Quality of life

→ Preparing Patients/Families/Caregiver(s) for End-of-Life and Transition to Hospice Care (See PAL-27)
Advance Care Planning (See PAL-29)

Symptom management[f] →
- Pain → Pain Interventions (See PAL-10)
- Dyspnea → Dyspnea Interventions (See PAL-11)
- Anorexia/cachexia → Anorexia/Cachexia Interventions (See PAL-13)
- Nausea/vomiting (NV) → Nausea/Vomiting Interventions (See PAL-15)
- Constipation → Constipation Interventions (See PAL-17)
- Diarrhea → Diarrhea Interventions (See PAL-18)
- Malignant bowel obstruction → Malignant Bowel Obstruction (See PAL-20)
- Fatigue/weakness/asthenia → See NCCN Guidelines for Cancer-Related Fatigue
- Insomnia/sedation → Insomnia/Sedation Interventions (See PAL-22)
- Delirium → Delirium Interventions (See PAL-23)

[f]Look for opportunities to use single agents to treat multiple symptoms.

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ASSESSMENT BY ONCOLOGY TEAM

Psychosocial distress

- **Psychosocial/psychiatric[f]**
  - **Depression/anxiety**
  - **Distress**

  → See NCCN Guidelines for Distress Management
- **Spiritual or existential needs** → Consider Consultation with Palliative Care Specialist (See PAL-8)
- **Social support challenges or concerns**
  - **Home**
  - **Family**
  - **Community**
- **Resource needs**

  → Social Support/Resource Management (See PAL-25)

- **Educational and informational needs**
- **Cultural factors affecting care**

→

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

→ Preparing Patients/Families/Caregivers for End-of-Life and Transition to Hospice Care (See PAL-27)

Criteria for consultation with palliative care specialist → (See PAL-7)

[f]Look for opportunities to use single agents to treat multiple symptoms.

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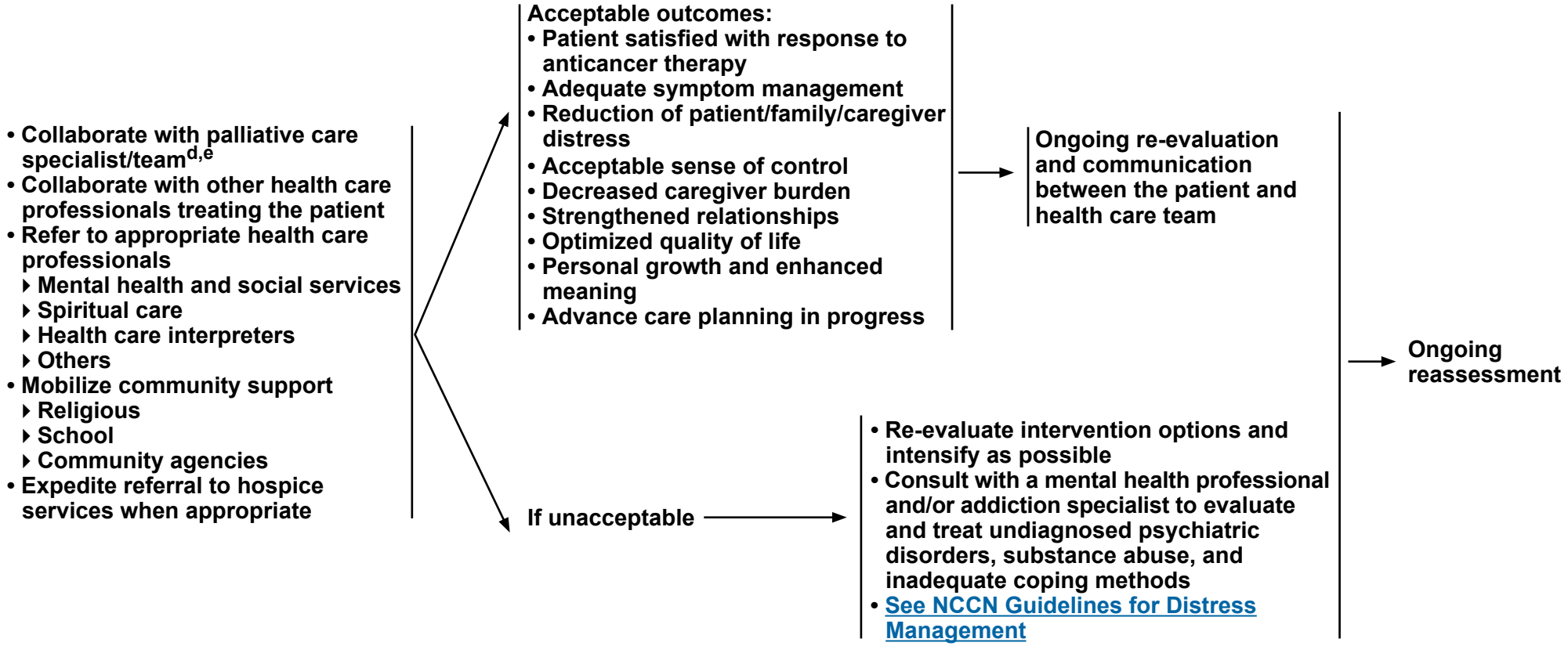
ONCOLOGY TEAM INTERVENTIONS **REASSESSMENT**



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CRITERIA FOR CONSULTATION WITH PALLIATIVE CARE SPECIALIST

ASSESSMENT

Patient characteristics →

- Patient with life-limiting cancer diagnosis
- Limited anticancer treatment options due to:
  - Limited access to anticancer treatment
  - Advanced disease process
  - Multiple and/or severe comorbid conditions
  - Rapidly progressive functional decline or persistently poor performance status
- Need for clarification of goals of care
- Resistance to engage in advance care planning
- High risk of poor pain management or pain that remains resistant to conventional interventions, eg:
  - Neuropathic pain
  - Incident or breakthrough pain
  - Pain with severe associated psychosocial and/or family distress
  - Rapid escalation of opioid dose
  - Multiple drug "allergies" or a history of multiple adverse reactions to pain and symptom management interventions
  - Concerns regarding drug or alcohol abuse — see addiction specialist as needed (See NCCN Guidelines for Adult Cancer Pain)
- High non-pain symptom burden, especially those resistant to conventional management (See PAL-4 for symptoms)
- High distress score (>4) (See NCCN Guidelines for Distress Management)
- Need for invasive procedures (eg, palliative stenting or venting gastrostomy)
- Frequent emergency department visits or hospital admissions
- Need for ICU-level care (especially involving multi-organ system failure or prolonged mechanical support)
- Communication barriers
  - Language
  - Literacy
  - Physical barriers
  - Cognitive impairment
- Request for hastened death

→ See Oncology Team Interventions (PAL-6)

Continued

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CRITERIA FOR CONSULTATION WITH PALLIATIVE CARE SPECIALIST

ASSESSMENT

Complex patient/family/caregiver circumstances →

- Family/caregiver challenges
- High risk for persistent complex bereavement disorder[g]
- Inadequate social support
- Substance abuse
- Intensely dependent relationship(s)
- Financial limitations
- Limited access to care
- Family discord
- Spiritual or existential crisis
- Unresolved or multiple prior losses
- Patient's concerns regarding family/caregiver well-being
  - Dependent children and/or older relatives requiring care living in the household

→ See Oncology Team Interventions (PAL-6)

Oncology care team/staff challenges →

- Complex care coordination issues within and among multiple care teams
- Compromised resilience including:
  - Compassion fatigue
  - Moral distress
  - Burnout

[g]Persistent complex bereavement disorder is a chronic heightened state of mourning that significantly impairs functioning.

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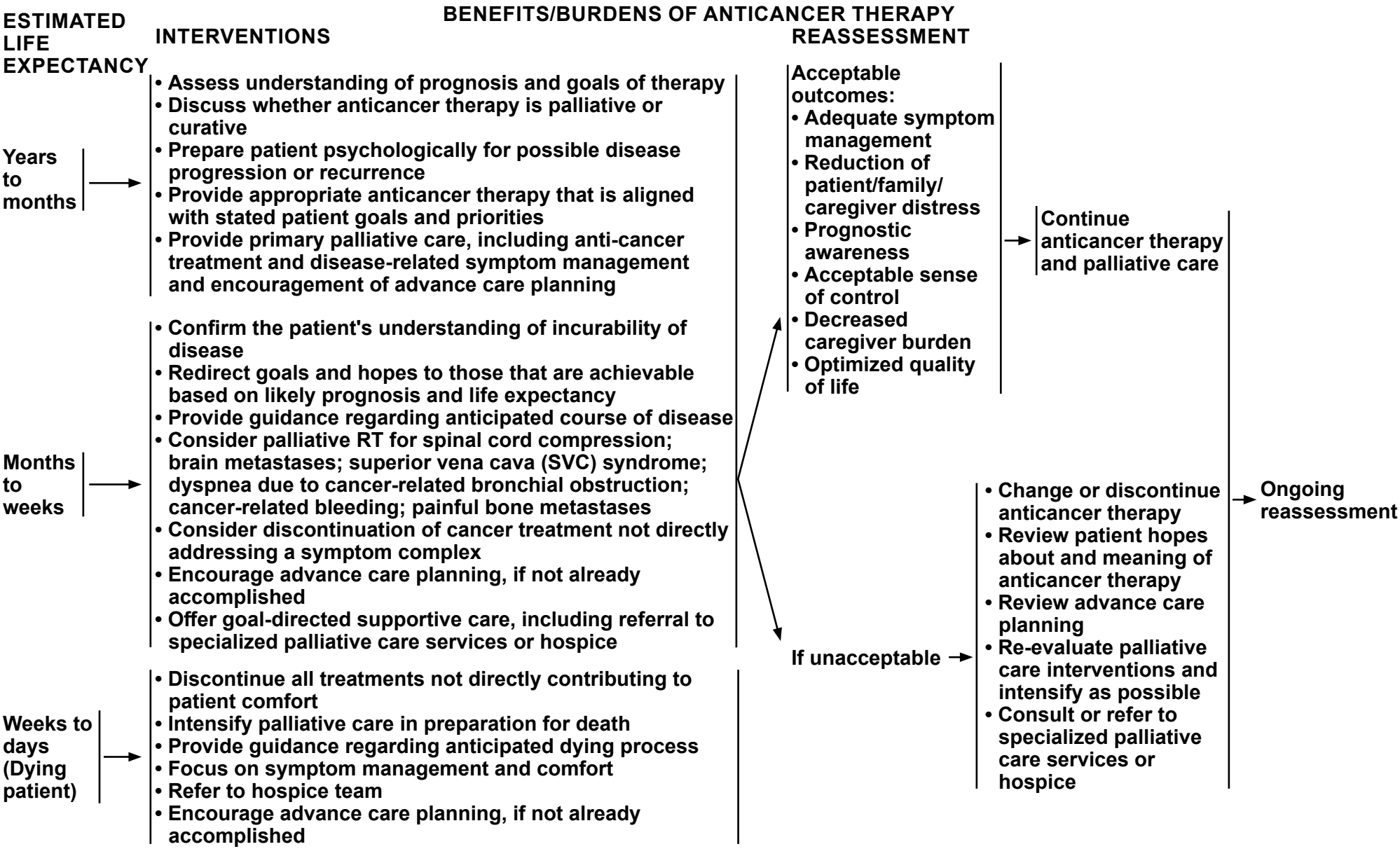

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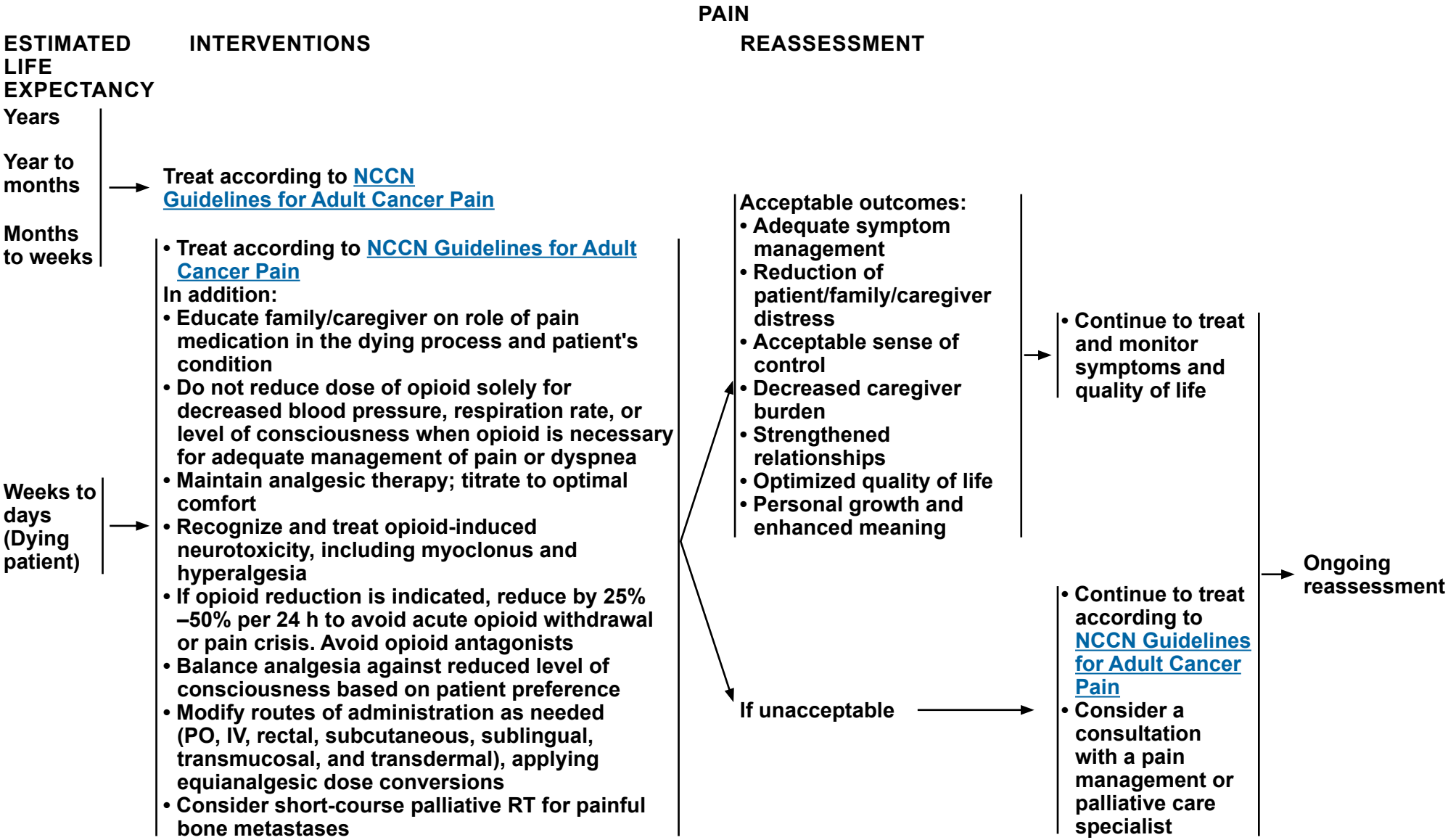

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ESTIMATED LIFE EXPECTANCY

INTERVENTIONS[h]

- Assess symptoms comprehensively
- Educate patient/family/caregiver on patient's condition and risk/benefit of treatment options
- Treat potentially reversible underlying causes/comorbid conditions:
  - Radiation/chemotherapy
  - Therapeutic procedure for cardiac, pleural, or abdominal fluid
  - Bronchoscopic therapy
  - Bronchodilators, diuretics, steroids, antibiotics, or transfusions
  - Anticoagulants for pulmonary emboli
- Relieve symptoms
  - Oxygen therapy for symptomatic hypoxia
  - Educational, psychosocial, and emotional support for the patient/family/caregiver
  - Nonpharmacologic therapies, including fans, cooler temperatures, stress management, relaxation therapy, and physical comfort measures
  - Pharmacologic therapy
    - ◊ Opioids[i]
    - ◊ Consider benzodiazepines if coexisting anxiety[j]
  - Noninvasive positive-pressure ventilation (eg, CPAP, BiPAP) support if clinically indicated for severe reversible condition
  - Consider palliative RT for SVC syndrome or respiratory obstruction by tumor mass

DYSPNEA REASSESSMENT

Acceptable outcomes:
- Adequate dyspnea and symptom management
- Reduction of patient/family/caregiver distress

→ **Continue to treat and monitor symptoms and quality of life**

→ **Ongoing reassessment**

If unacceptable →
- Re-evaluate palliative care interventions and intensify as possible
- Consult or refer to specialized palliative care services or hospice

Years

Year to months →

Months to weeks

Weeks to days (Dying patient) → See Interventions (PAL-12)

[h] See Drug Appendix (PAL-A) for specific recommendations for medical management of symptoms.

[i] For acute progressive dyspnea or for patients who are not opioid naive, more aggressive titration may be required.

[j] The addition of benzodiazepines to opioids can increase the risk of respiratory depression.

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DYSPNEA

ESTIMATED LIFE EXPECTANCY

Years

Year to months → See Interventions (PAL-11)

Months to weeks

Weeks to days (Dying patient) →

INTERVENTIONS[h]

- Assess symptoms comprehensively
  - Use labored breathing or other physical signs of dyspnea in noncommunicative patients
- Address patient/family/caregiver preferences, prognosis, reversibility of respiratory failure, and treatment options
- Provide anticipatory guidance for patient/family/caregiver regarding dying of respiratory failure
  - Consider time-limited trial of mechanical ventilation if indicated
- Provide emotional and spiritual support
- Focus on comfort
  - Continue to treat underlying condition as appropriate
- Relieve symptoms
  - Nonpharmacologic therapies
    - ◊ Educational, psychosocial, and emotional support (See PAL-11)
    - ◊ Fans, cooler temperatures
  - Pharmacologic therapies
    - ◊ Oxygen if hypoxic and/or subjective relief is reported
    - ◊ If opioid naive, morphine[k]
      - – If on chronic opioids, consider increasing dose by 25%
    - ◊ Benzodiazepines
  - If fluid overload is a contributing factor:
    - ◊ Decrease/discontinue enteral or parenteral fluid
    - ◊ Consider low-dose diuretics
- Reduce excessive secretions[l] with anti-secretory agents

REASSESSMENT

Acceptable outcomes:
- Adequate dyspnea and symptom management
- Reduction of patient/family/caregiver distress

→ Continue to treat and monitor symptoms and quality of life

If unacceptable →
- Re-evaluate palliative care interventions and intensify as possible
- Consider a consultation with a palliative care specialist
- Consider sedation for intractable symptoms (See PAL-33)

→ Ongoing reassessment

[h] See Drug Appendix (PAL-A) for specific recommendations for medical management of symptoms.

[k] For acute progressive dyspnea or for patients who are not opioid naive, more aggressive titration may be required.

[l] Hughes A, et al. Audit of three antimuscarinic drugs for managing retained secretions. Palliat Med 2000;14:221-222.

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

ANOREXIA/CACHEXIA

ESTIMATED LIFE EXPECTANCY

ASSESSMENT AND INTERVENTIONS[h]

- Evaluate rate/severity of weight loss and associated symptoms
- Educate patient/family/caregiver on patient's condition and risk/benefits of treatment options
- Conditions/symptoms that interfere with intake
  - Dysgeusia
  - Xerostomia
  - Mucositis
  - Oral-pharyngeal candidiasis
  - Depression
  - Early satiety (if gastroparesis: try metoclopramide)
  - Nausea/vomiting (NV) (See PAL-15)
  - Dyspnea (See PAL-11)
  - Constipation (See PAL-17)
  - Pain (See NCCN Guidelines for Adult Cancer 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 an exercise program designed to enhance mobility and conserve energy
- Assess social and economic factors
- Consider nutrition consult
- Consider nutrition support, enteral and parenteral feeding (as appropriate)

Years to Year to months →

Months to weeks

Weeks to days (Dying patient) → See Interventions (PAL-14)

REASSESSMENT

Acceptable outcomes:
- 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**

→ **Ongoing reassessment**

If unacceptable →
- Re-evaluate palliative care interventions and intensify as possible
- Provide dietary consultation
- Consider appetite stimulant

[h] See Drug Appendix (PAL-A) for specific recommendations for medical management of symptoms.

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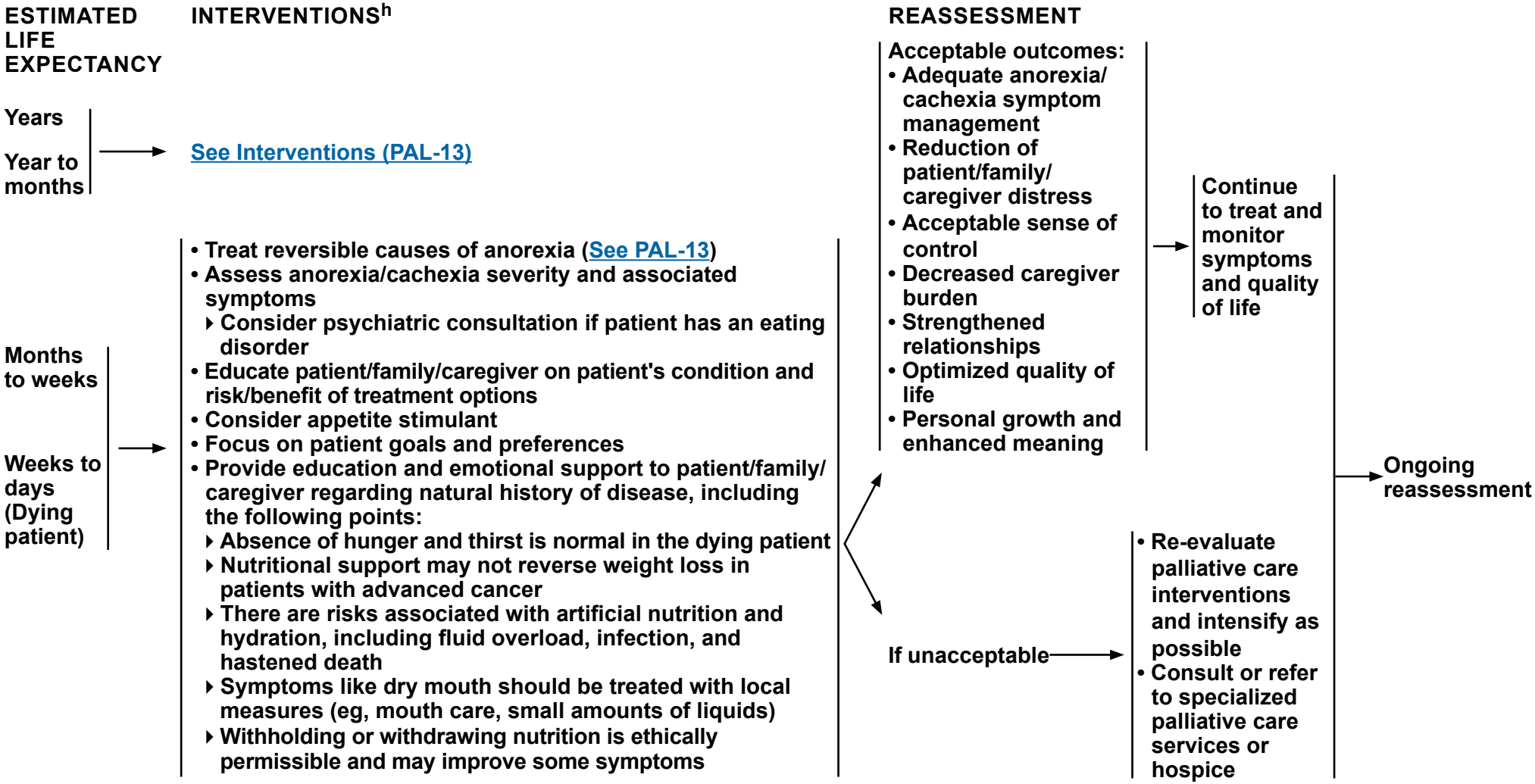
ANOREXIA/CACHEXIA



[h] See Drug Appendix (PAL-A) for specific recommendations for medical management of symptoms.

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NAUSEA AND VOMITING

INTERVENTIONS[h]

- Assess NV severity and associated symptoms
- Educate patient/family/caregivers on patient's condition and treatment options
- Chemotherapy/radiation therapy-induced (See NCCN Guidelines for Antiemesis)
- Severe constipation/fecal impaction (See PAL-17)
- Gastroparesis
  - Prokinetic agent
- Bowel obstruction (See PAL-20)
- Central nervous system (CNS) involvement
  - Corticosteroids
  - Palliative radiation therapy
- Gastric outlet obstruction from intra-abdominal tumor or liver metastasis
  - Consider treatment with corticosteroids, a proton pump inhibitor, and metoclopramide
  - Endoscopic stenting
  - Decompressing G-Tube
- Gastritis/GERD
  - Proton pump inhibitor
  - H2-blocker
- Treat other causes (hypercalcemia, uremia, dehydration)

- Medication/substance-induced
  - Review medication list, including non-prescribed supplements and herbs, and discontinue any unnecessary medications
  - Review use of marijuana/cannabis for possible cannabis-associated hyperemesis syndrome and counsel regarding cessation if indicated.
  - Check available blood levels of necessary medications (eg, digoxin, phenytoin, carbamazepine, tricyclic antidepressants)
  - Treat medication-induced gastropathy (eg, proton pump inhibitor, prokinetic agent)
  - Consider rotating and/or reducing opioid requirement with non-nauseating coanalgesics or procedural interventions
- Psychogenic
  - Consider psychiatric consultation if patient has an eating disorder, somatization, phobia, or panic disorder causing NV. See NCCN Guidelines for Distress Management
- Non-specific NV
  - Initiate pharmacologic management with dopamine receptor antagonists or 5-HT3 receptor antagonists
  - If anxiety contributes to NV, consider adding benzodiazepine
  - If vertiginous component, consider anticholinergic/antihistamine
  - Consider non-pharmacologic therapies, such as acupuncture, hypnosis, and cognitive behavioral therapy

If NV stops:
See Reassessment (PAL-16)

If NV persists:
See Interventions (PAL-16)

[h] See Drug Appendix (PAL-A) for specific recommendations for medical management of symptoms.

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PERSISTENT NAUSEA AND VOMITING

INTERVENTIONS[h,m,n]

- Titrate dopamine antagonist to maximum benefit and tolerance.
- For continued NV, consider additional drug classes with potential antiemetic properties: See drug appendix (PAL-A)
  - Corticosteroid
  - 5-HT3 antagonist
  - Antipsychotic
  - Anticholinergic
  - Antihistamine
  - Oral cannabinoid
  - Antidepressant (mirtazapine)

- Consider appropriate route of administration
  - Prescribe oral, sublingual, or rectal agent and titrate to maximum benefit; consider opioid rotation
  - If NV persists, provide PRN, scheduled, or continuous parenteral infusion as necessary
  - Consider subcutaneous administration as an alternative

REASSESSMENT

Acceptable outcomes:
- Adequate NV symptom management
- Reduction of patient/family/caregiver distress
- Acceptable sense of control
- Decreased caregiver burden
- Optimized quality of life

→ Continue to treat and monitor symptoms and quality of life

→ Ongoing reassessment (See Interventions, PAL-15)

If unacceptable →
- Re-evaluate palliative care interventions and intensify as possible
- Consult or refer to specialized palliative care services or hospice
- Consider palliative sedation (See PAL-33)

[h] See Drug Appendix (PAL-A) for specific recommendations for medical management of symptoms.
[m] An around-the-clock dosing schedule may provide the most consistent benefit to the patient.
[n] Continuous intravenous or subcutaneous infusions of different antiemetics may be necessary for the management of intractable NV.

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CONSTIPATION[1,2]

Preventive measures[h]
- Increase fluids
- Increase dietary fiber if patient has adequate fluid intake and physical activity
- Exercise, if appropriate
- Administer prophylactic medications
  - Stimulant laxative ± osmotic laxative
  - Increase laxative dose with goal of 1 non-forced bowel movement (BM) every 1–2 days

INTERVENTIONS[h]

If constipation is present:
- Educate patient/family/caregivers on patient's condition and treatment options
- Assess for cause and severity of constipation
  - Discontinue any non-essential constipating medication
- 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 stimulant and/or osmotic laxative

If impacted:
- Administer glycerine suppository ± mineral oil retention enema[o]
- 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
- Consider peripherally acting mu-opioid receptor antagonist (PAMORA) for opioid-induced constipation
  - Avoid if concern for post-op ileus and/or mechanical bowel obstruction
- Administer tap water enema until clear
- Consider use of a prokinetic agent

REASSESSMENT

Acceptable outcomes:
- Adequate constipation symptom management
- Reduction of patient/family/ caregiver distress

→ Continue to treat and monitor symptoms and quality of life

If unacceptable →
- Re-evaluate palliative care interventions and intensify as possible
- Consult or refer to specialized palliative care services or hospice

Ongoing reassessment

[h] See Drug Appendix (PAL-A) for specific recommendations for medical management of symptoms.
[o] Use suppository and enema with caution in patients receiving chemotherapy due to risk of cytopenia.

[1] Wickham RJ. Managing constipation in adults with cancer. J Adv Pract Oncol 2017;8(2):149-161.
[2] Larkin PJ, Cherny NI, LaCarpia D, et al. Diagnosis, assessment and management of constipation in advanced cancer: ESMO Clinical Practice Guidelines. Ann Oncol 2018; 29 (Suppl 4):iv111-iv125.

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DIARRHEA

INTERVENTIONS/FURTHER ASSESSMENT

SCREENING AND ASSESSMENT
- Evaluate diarrhea severity and cause
- Educate patient/family/caregiver on condition and treatment options

SEVERITY
Determine Diarrhea Grade[p]

- Grade 1: Increase of <4 stools/day over baseline; mild increase in ostomy output
- Grade 2: Increase of 4–6 stools/day over baseline; moderate increase in ostomy output
- Grade 3: Increase of >7 stools/day over baseline; incontinence; hospitalization indicated; severe increase in ostomy output; limiting self-care; interferes with activities of daily living (ADLs)
- Grade 4: Life-threatening consequences; urgent intervention indicated

→

- Provide immediate antidiarrheal therapy indicated by grade
- If chemotherapy induced, decrease or delay the next dose of chemotherapy
- Tailor treatment to potential causes
  - IBS/Crohn's disease
  - Post-surgical/anatomic changes (ie, short bowel syndrome)
  - Recent antibiotic use
  - Chemotherapy regimen
  - RT side effects
    OR
    Radiation-induced enteritis or other adverse effects
  - Drugs that frequently induce diarrhea
  - GVHD and/or immunotherapy-related colitis
  - Pancreatic insufficiency in pancreatic cancer
  - Dietary changes
  - Infection
    - ◊ Screen for C. diff, HIV, and other comorbid infections (ie, ova/parasites)
- If fecal impaction is suspected, See PAL-17

→

See Anti-Diarrheal Interventions, Grades 1-4 (PAL-19)

[p]NCI Table 3: http://www.cancer.gov/cancertopics/pdq/supportivecare/gastrointestinalcomplications/HealthProfessional/page5#section_5.8

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ANTIDIARRHEAL INTERVENTIONS

SCREENING

- **Provide immediate antidiarrheal therapy indicated by grade**

INTERVENTION[h]

GRADE 1 →

- **If chemotherapy induced, decrease or delay the next dose of chemotherapy**
- **Provide oral hydration and electrolyte replacement**
- **Initiate antidiarrheal (eg, diphenoxylate/atropine) if patient not already on opioids**

GRADE 2 →

- **Provide IV fluids if patient is unable to tolerate oral fluids**
- **Initiate/continue antidiarrheal—as above**
- **Consider anticholinergic agents**
- **If non-C.diff infection-related: Treat with appropriate antibiotics**
- **If C. diff infection-related: Administer antibiotics and probiotics as appropriate**
- **If chemotherapy-induced, decrease or delay the next dose of chemotherapy**
- **If immunotherapy-mediated diarrhea, consider**
  - **Corticosteroids**
  - **Infliximab**
  - **Probiotics**
  - **See Management of Immunotherapy Related Toxicity Guidelines for immunotherapy-related diarrhea**

GRADES 3/4 →

- **Inpatient hospitalization (intensive care for Grade 4 if consistent with goals)**
- **For GVHD diarrhea, consider limiting diet, steroids, and IV nutrition**
- **Provide IV fluids and use antidiarrheal agents and anticholinergics as mentioned above**
- **Consider somatostatin analog**
- **Consider parenteral hydration in home setting**

[h] See Drug Appendix (PAL-A) for specific recommendations for medical management of symptoms.

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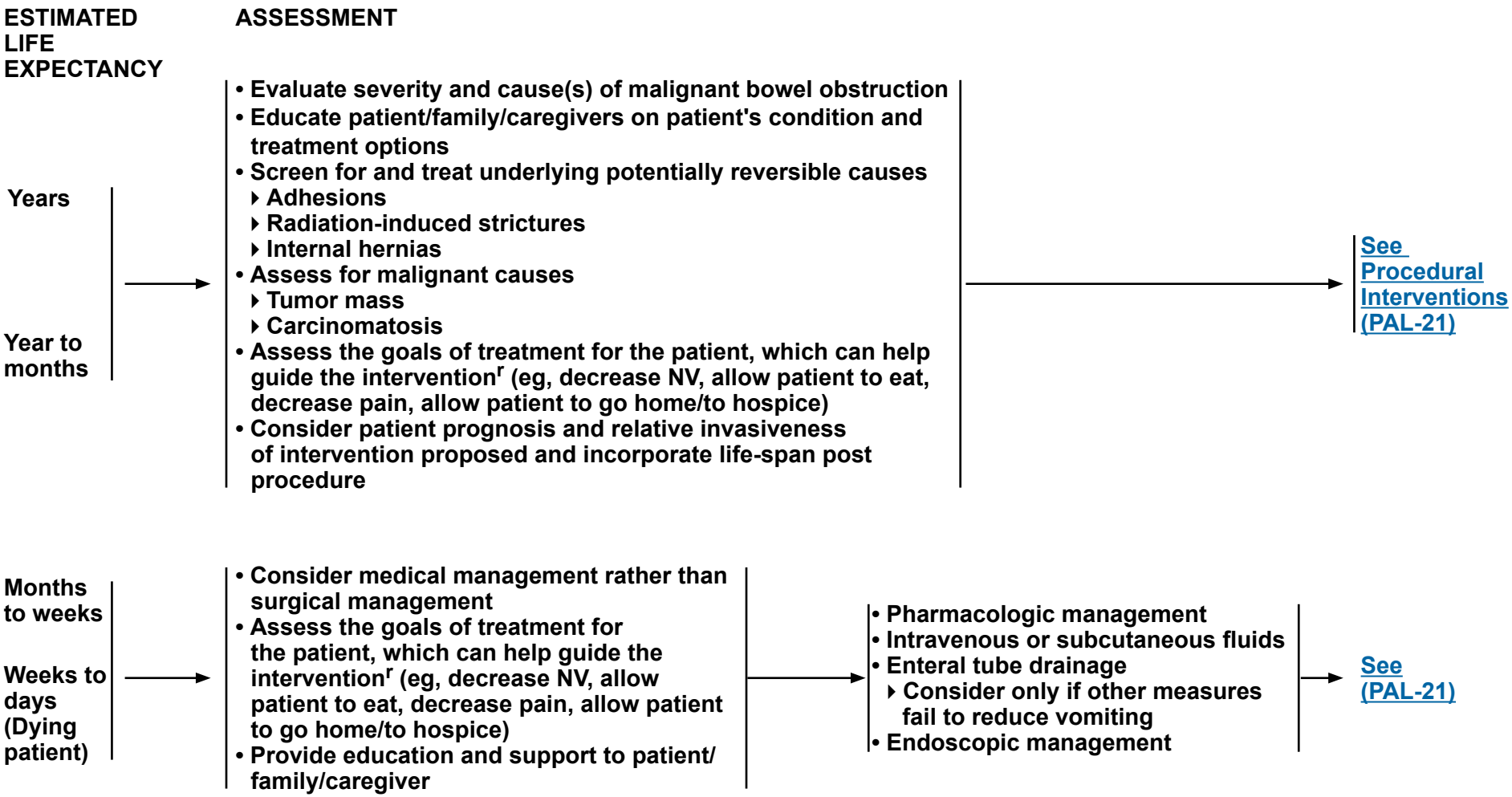
MALIGNANT BOWEL OBSTRUCTION[q]



[q]Plain film radiography may be helpful in confirming the clinical diagnosis of bowel obstruction. Consider a CT scan if surgical intervention is contemplated, as it is more sensitive and may help identify the cause of obstruction.
[r]Most malignant bowel obstructions are partial, allowing time to discuss appropriate intervention with the patient/family/caregiver.

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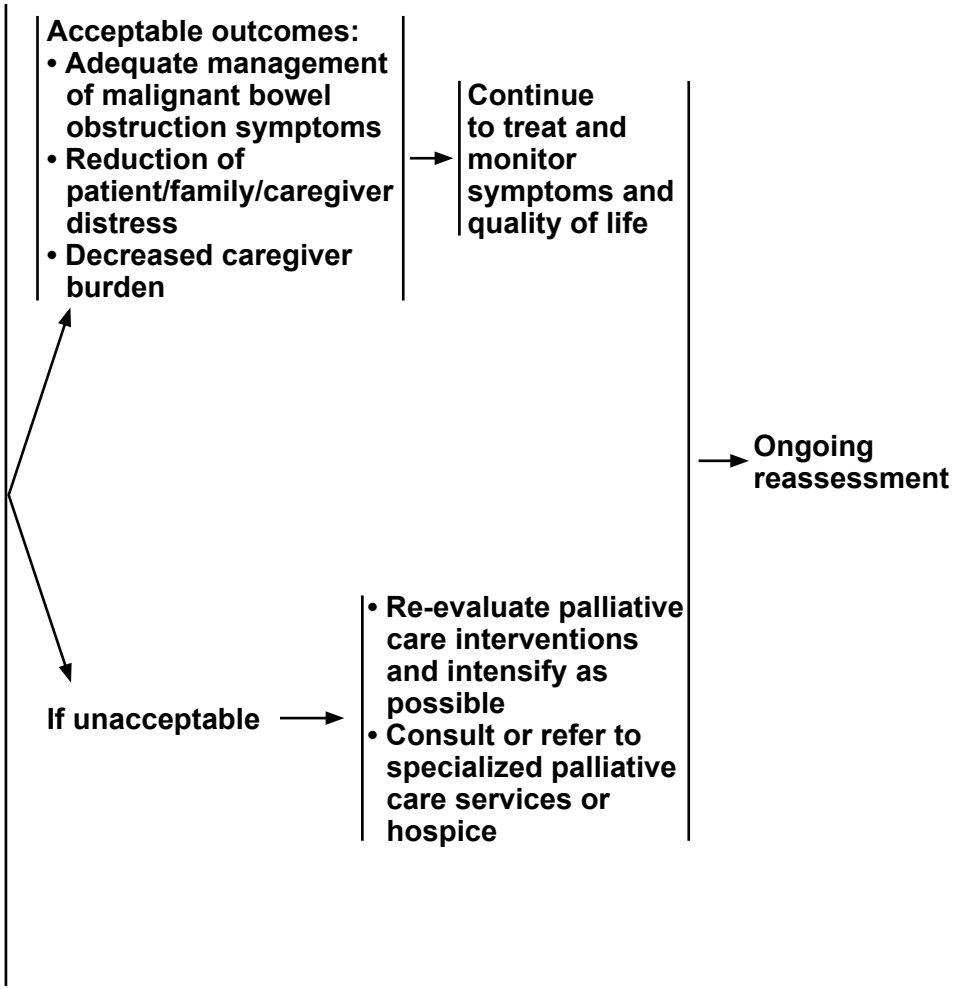
MALIGNANT BOWEL OBSTRUCTION

PROCEDURAL INTERVENTIONS[h]

- Operative management
  - Discuss treatment options with patient/family/caregiver
    - ◊ Risk of mortality, morbidity, and re-obstruction
    - ◊ Overall prognosis
    - ◊ Invasiveness of the proposed intervention
- Risk factors for poor surgical outcome include ascites, carcinomatosis, palpable intra-abdominal masses, multiple bowel obstructions, previous abdominal radiation, very advanced disease, and poor overall clinical status
- Endoscopic management
  - Percutaneous endoscopic gastrostomy tube for drainage
  - Endoscopic stent placement
- Interventional radiology management
  - Gastrostomy tube for drainage
- Pharmacologic management when the goal is maintaining gut function:
  - Use rectal, transdermal, subcutaneous, or intravenous routes of administration
  - Opioids
  - Antiemetics: Do not use antiemetics that increase gastrointestinal mobility such as metoclopramide; however, these may be beneficial in incomplete bowel obstruction
  - Corticosteroids
- Pharmacologic management when gut function cannot be maintained:
  - Administer antisecretory agents
  - Intravenous or subcutaneous fluids
- Nasogastric or gastric tube drainage
  - Increased risk of aspiration
  - Consider a limited trial only if other measures fail to reduce vomiting
- Total parenteral nutrition (TPN)
  - Consider only if there is expected improvement of quality of life and life expectancy of months to years

REASSESSMENT



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SLEEP/WAKE DISTURBANCES INCLUDING INSOMNIA AND SEDATION

ESTIMATED LIFE EXPECTANCY

ASSESSMENT AND INTERVENTIONS[h]

- Educate patient/family/caregivers on patient's condition and treatment options
- Evaluate type/severity of sleep-wake disturbance, including daytime impairments (eg, Epworth Sleepiness Scale)
- Explore fears and anxiety regarding death/disease
- Provide sleep-hygiene education
- Provide cognitive-behavioral treatment
  - Includes stimulus control, progressive muscle relaxation
- Consider polysomnography if history is suggestive 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 and periodic limb movement disorder
    - ◊ CPAP/BiPAP
  - Restless legs syndrome
- Provide pharmacologic therapies for refractory sleep/wake disturbance
  - Insomnia:
    - ◊ Antipsychotics
    - ◊ Sedative/hypnotics
    - ◊ Benzodiazepines
    - ◊ Antidepressants
    - ◊ Alpha adrenergic blockers
    - ◊ Melatonin-receptor agonists
  - Daytime sedation:
    - ◊ CNS stimulant/wakefulness-promoting agents

REASSESSMENT

Years

See NCCN Guidelines for Survivorship

Year to months

Months to weeks

→ **Acceptable outcomes:**
- Adequate management of symptoms
- Reduction of patient/family/caregiver distress

→ **Continue to treat and monitor symptoms and quality of life**

→ **Ongoing reassessment**

If unacceptable →
- Re-evaluate contributing etiologies
- Change insomnia or antisedation therapy
- Re-evaluate palliative care interventions and intensify as possible
- Consult or refer to specialized palliative care services or hospice

Weeks to days (Dying patient) →
- Assess patient's desire to have insomnia and sedation treated
- Adjust doses of pharmacologic therapies
  - Consider chlorpromazine

[h] See Drug Appendix (PAL-A) for specific recommendations for medical management of symptoms.

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DELIRIUM

ESTIMATED LIFE EXPECTANCY

Years

Year to months

Months to weeks

Weeks to days (Dying patient) → See Interventions (PAL-24)

INTERVENTIONS[h]

- Evaluate delirium severity and cause (eg, DSM criteria) See also NCCN Guidelines for Distress Management
  - Hyperactive
  - Hypoactive
- Educate patient/family/caregivers on patient's condition and treatment options
- Screen for and treat underlying reversible causes
  - Metabolic causes and medication withdrawal
  - Dehydration
  - Unrelieved pain
  - Hypoxia
  - Bowel obstruction/obstipation
  - Infection
  - Brain metastases (consider palliative RT) or other CNS events
  - Bladder outlet obstruction
  - Medication or substance effect or withdrawal (eg, benzodiazepines, opioids, anticholinergics, non-prescribed substances)
- Assess, screen for, and maximize nonpharmacologic interventions (eg, reorientation, cognitive stimulation, sleep hygiene)

Severe delirium (agitation) →
- Reduce or eliminate delirium-inducing medications as possible (eg, steriods, anticholinergics, benzodiazepines)
- Administer haloperidol
- Administer alternative antipsychotic medications
- If agitation is refractory to high doses of neuroleptics, consider adding benzodiazepine
- Titrate starting dose to optimal effect with lowest possible dose
- Consider opioid dose reduction or rotation
- Support caregivers

Mild/moderate delirium →
- Administer haloperidol
- Administer alternative antipsychotic medications
- Titrate starting dose to optimal effect with lowest possible dose
- Orient patient with family/caregiver(s) presence
- Support caregivers

REASSESSMENT

Acceptable outcomes:
- Adequate delirium symptom management
- Reduction of patient/family/caregiver distress
- Decreased caregiver burden

→ Continue to treat and monitor symptoms and quality of life → Ongoing reassessment

If unacceptable →
- Re-evaluate palliative care interventions and intensify as possible
- Consider consultation with a palliative care specialist or psychiatrist

[h] See Drug Appendix (PAL-A) for specific recommendations for medical management of symptoms.

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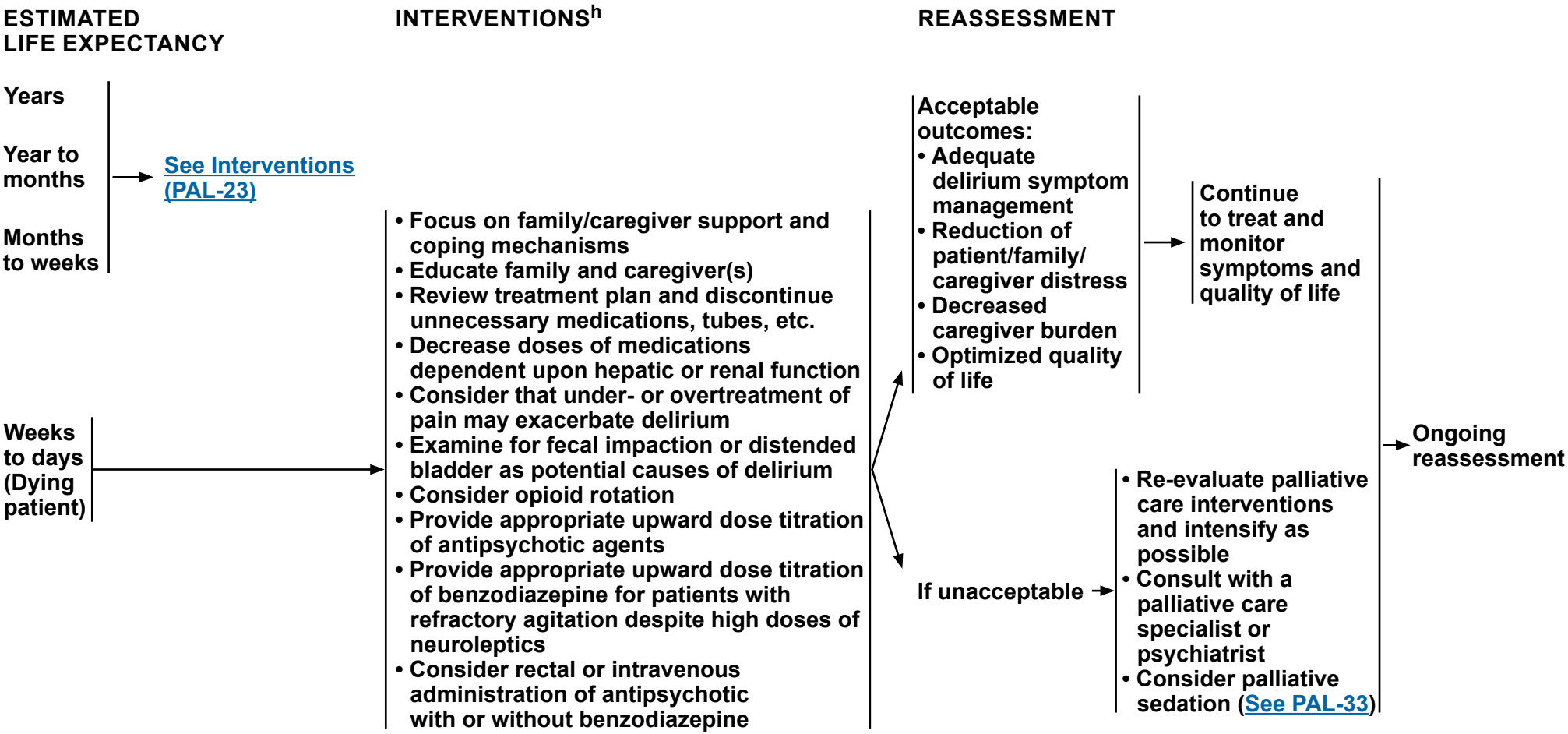
DELIRIUM



[h] See Drug Appendix (PAL-A) for specific recommendations for medical management of symptoms.

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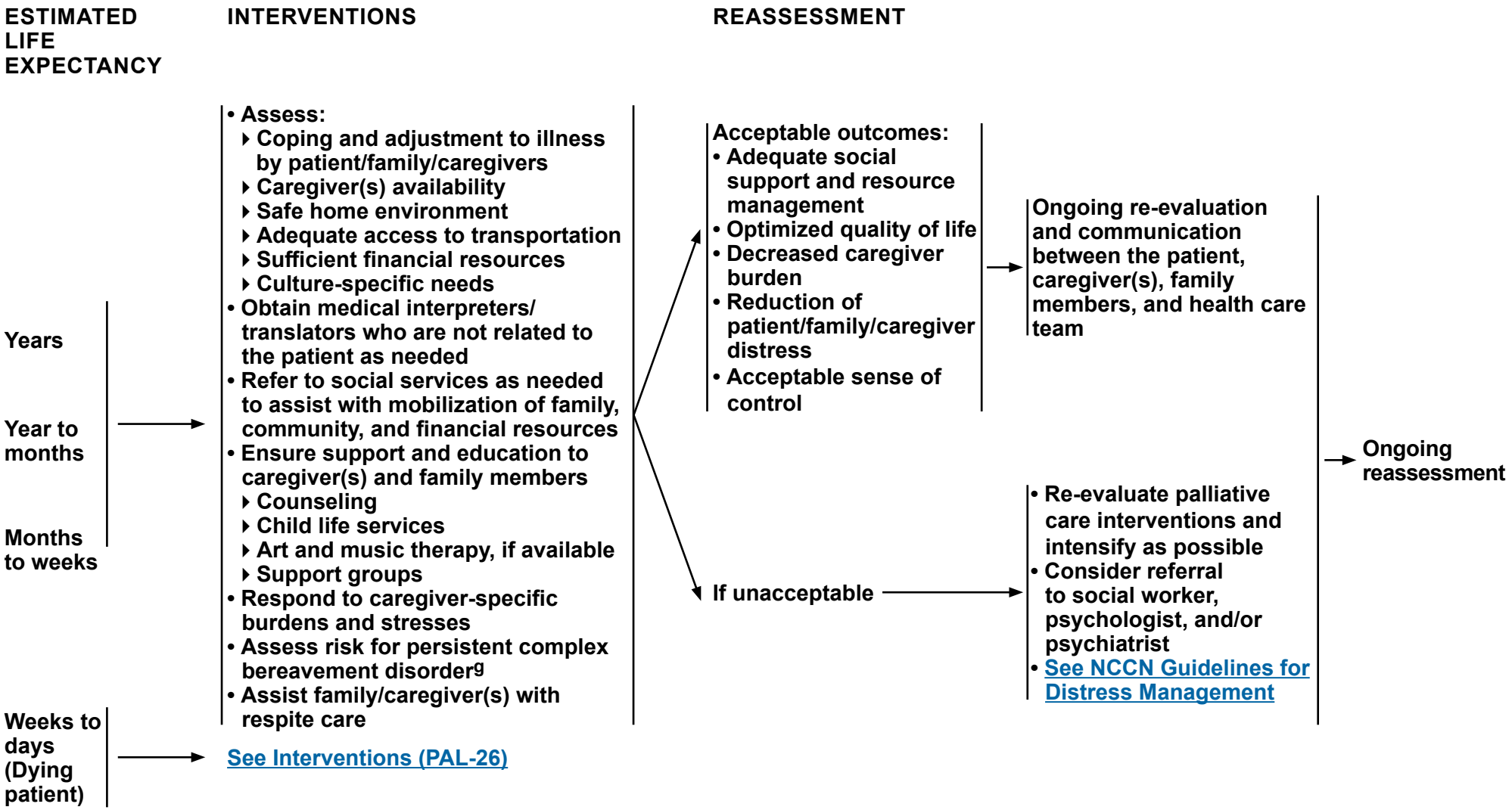
SOCIAL SUPPORT/RESOURCE MANAGEMENT



[g]Persistent complex bereavement disorder is a chronic heightened state of mourning that significantly impairs functioning.

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SOCIAL SUPPORT/RESOURCE MANAGEMENT

ESTIMATED LIFE EXPECTANCY

Years

Year to months → See Interventions (PAL-25)

Months to weeks

Weeks to days (Dying patient) →

INTERVENTIONS

- Assess prognostic awareness and discuss prognosis on an ongoing basis with the patient/family/caregiver(s)
- Evaluate and support the patient's desires for comfort
- Explain the dying process and expected events to the patient/caregiver(s)/family members
- Respond to caregiver-specific demands and stresses
- Assess risk for persistent complex bereavement disorder[g]
- Ensure that care conforms with cultural and spiritual/religious practices
- Provide emotional support and address any patient-family or intra-family conflicts regarding intervention
- Child life services if available
- Art and music therapy if available
- 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, readiness, and need for specialized palliative or hospice care

REASSESSMENT

Acceptable outcomes:
- Adequate social support and resource management
- Optimized quality of life
- Decreased caregiver burden
- Reduction of patient/family/caregiver distress
- Acceptable sense of control

→ **Ongoing re-evaluation and communication between the patient and health care team**

→ **Ongoing reassessment**

If unacceptable →
- Re-evaluate palliative care interventions and intensify as possible
- Consult or refer to specialized palliative care services, hospice, or ethics committee
- Consider referral to social worker, psychologist, and/or psychiatrist
- See NCCN Guidelines for Distress Management

[g]Persistent complex bereavement disorder is a chronic heightened state of mourning that significantly impairs functioning.

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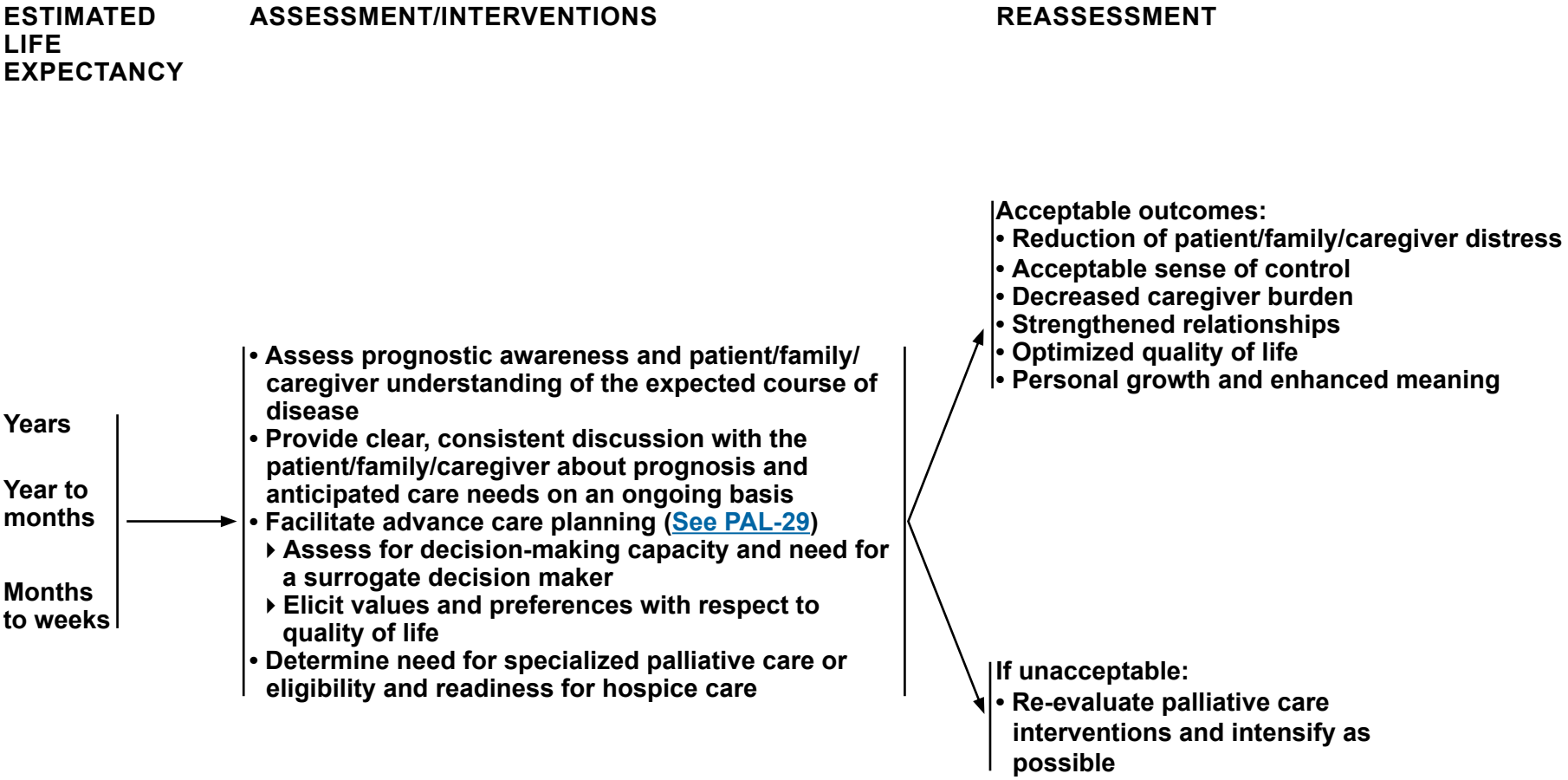
PREPARING PATIENTS/FAMILIES/CAREGIVERS FOR END-OF-LIFE AND TRANSITION TO HOSPICE CARE



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PREPARING PATIENTS/FAMILIES/CAREGIVERS FOR END-OF-LIFE AND TRANSITION TO HOSPICE CARE

ESTIMATED LIFE EXPECTANCY

Years

Year to months → See Interventions (PAL-27)

Months to weeks

Weeks to days (Dying patient) →

- Educate patient/family/caregiver on dying process
- Address potential need for transitions in care while ensuring continued involvement of primary care physician and primary oncology team
- Refer to hospice care agencies
- Provide information and additional referrals, as necessary, for:
  - ▸ Psychosocial assessment
    - ◊ Legacy work
    - ◊ Grief counseling
  - ▸ Spiritual assessment
    - ◊ Spiritual support if needed
  - ▸ Funeral/memorial service planning
- Respect goals and needs of the patient/family/caregiver regarding the dying process

REASSESSMENT

Acceptable outcomes:
- Reduction of patient/family/caregiver distress
- Acceptable sense of control
- Decreased caregiver burden
- Optimized quality of life

If unacceptable:
- Re-evaluate palliative care interventions and intensify as possible

→ Ongoing reassessment (See PAL-27)

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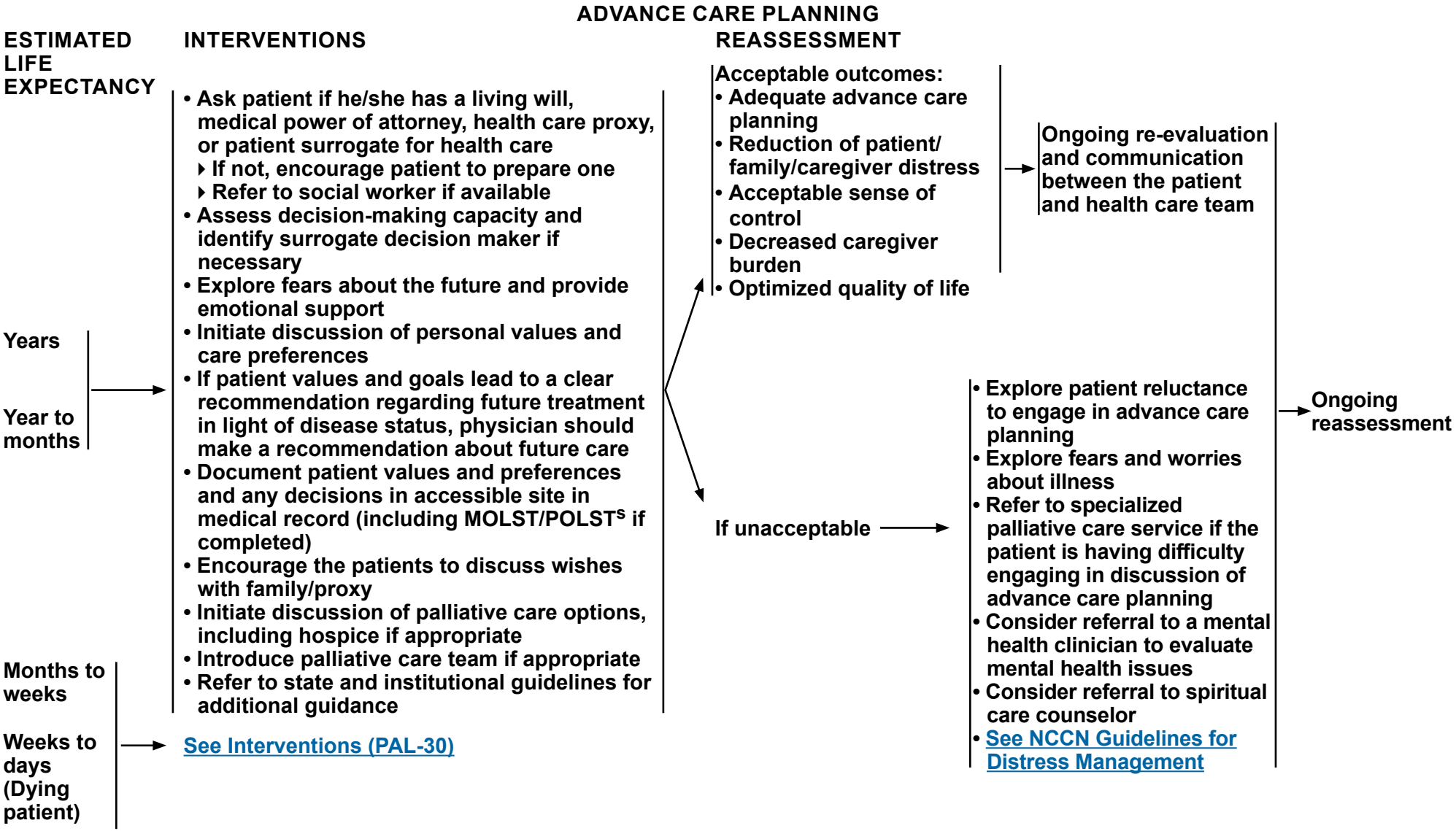

[s]Patient's values and preferences and any decisions should be documented in the medical record, including MOLST/POLST (Medical Orders for Life-Sustaining Treatment or Physician Orders for Life-Sustaining Treatment).

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ADVANCE CARE PLANNING

ESTIMATED LIFE EXPECTANCY

Years → • See Interventions (PAL-29)

Year to months

INTERVENTIONS

- Address years-to-months interventions
- Determine patient/family/caregiver preferences for the location of the patient's death
- Confirm the patient's values and decisions in light of changes in status
- If not previously done, make recommendations about appropriate medical treatment to meet the patient's values and goals
- Ensure complete documentation of the advance care plan in the medical record, including MOLST/POLST[s] if applicable, to assure accessability of the plan to all clinicians across care settings
- Explore family/caregiver concerns about the patient's plan and seek resolution of conflict between patient/family/caregiver goals and wishes
- Consider consultation with a palliative care specialist to assist in conflict resolution when the patient, family, and health care team disagree
- Explore fears about dying and address concerns

Months to weeks →

- Assure that all items identified above are complete
- Implement and ensure compliance with advance care plan
- Clarify and confirm patient and family decisions about life-sustaining treatments, including CPR, if necessary
- Explore desire for organ donation and/or autopsy
- Encourage the patient/family/caregiver as appropriate to avoid CPR using do not resuscitate (DNR)/do not attempt resuscitation (DNAR)/allow natural death (AND) orders

Weeks to days (Dying patient) →

REASSESSMENT

Acceptable outcomes:

- Adequate advance care planning
- Reduction of patient/family/caregiver distress
- Acceptable sense of control
- Decreased caregiver burden
- Optimized quality of life

→ Ongoing re-evaluation and communication between the patient/family/caregiver and health care team

If 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 Guidelines for Distress Management

→ Ongoing reassessment

[s]Patient's values and preferences and any decisions should be documented in the medical record, including MOLST/POLST (Medical Orders for Life-Sustaining Treatment or Physician Orders for Life-Sustaining Treatment).

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

RESPONSE TO REQUESTS FOR HASTENED DEATH (PHYSICIAN-ASSISTED DYING)

- We believe that a request for hastened death often has important meanings that require exploration. The most appropriate initial response to a request for hastened death is to intensify palliative care. Patients making such a request should be referred to a palliative care specialist. However, evaluating a patient's request for hastened death is an important skill, even for clinicians who feel this practice is never morally acceptable. Clarifying these meanings may enlarge the range of useful therapeutic options and might reduce the patient's wish to die.
- Explore the reasons for the request for a hastened death, and find out "why now" in a joint discussion with the patient, family, and caregivers.
  - Reassess symptom management.
  - Reassess psychological/psychiatric issues, especially depression, anxiety, grief, psychosis, delirium, and dementia.
  - Ask about the patient's relationship to family or other important people.
  - Ask about individual values and personal views of spiritual/existential suffering and consider spiritual care consultation for further exploration and intervention.
  - Assess for fears of caregiver burden and abandonment and re-emphasize physician commitment to the patient.
- 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.
- Request a consult with a mental health professional to evaluate and treat reversible causes of psychological suffering.
- Offer information about the natural history of the disease and explain the process of dying.
- Discuss the differences between withdrawal of life-sustaining nutrition/hydration, voluntary cessation of eating or drinking, and/or sedation for refractory symptoms.
- Address the role of medical caregivers, including hospice if appropriate.
- 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 requests for hastened death. 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, specialized 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, psychosocial, and spiritual distress. Re-emphasize your own commitment to providing continuing care for the patient. Re-evaluate and maintain medications for symptom management.

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CARE OF THE IMMINENTLY DYING HOSPITALIZED 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**
  - **Obtain hospice evaluation, if available**
  - **Intensify comfort measures**
    - ◊ **Implement skin safety protocol according to risk assessment:**
      - **Regularly reposition the patient for comfort as indicated**
      - **Reassess and premedicate for wound care as needed**
      - **Use a pressure-relieving mattress, if available**
      - **Provide eye and mouth care to maintain moisture**
      - **Treat for urinary retention and fecal impaction**
  - **Ensure deactivation of implanted defibrillator**
  - **Consider deactivation of implanted pacemaker in select patients**
  - **Discontinue unnecessary diagnostic tests and interventions such as transfusions, needle sticks, blood glucose monitoring, oxygen saturation monitoring, and suctioning**
  - **Replace check of vital signs with regular (eg, every 4 h) symptom assessments**
  - **Switch routes of medication administration when the oral route is no longer feasible**
  - **Adjust doses of medications to optimal comfort**
    - ◊ **Treat pain and fever**
  - **Treat unclearable terminal secretions (death rattle) by:**
    - ◊ **Reducing parenteral and enteral fluids**
    - ◊ **Repositioning the patient**
    - ◊ **Avoid deep suctioning**
  - **Treat dyspnea by adjusting the dose of medication (See PAL-11)**
  - **Treat delirium (See PAL-24)**
  - **Consider palliative sedation for refractory restlessness and agitation (See PAL-33)**
  - **Be prepared to discuss a request for organ donation and autopsy**
- **Psychosocial**
  - **Help support the patient/family/caregiver 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**
  - **Ensure that the family/caregiver understands 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 and provide education to parents on age-appropriate grieving process**
  - **Encourage visits by children if consistent with family values**
  - **Support cultural practices**
  - **Ensure that caregivers understand and will honor advance directives**
  - **Promote healthy grieving**
- **Practical**
  - **Mobilize in-hospital end-of-life care policies and procedures**
  - **Ensure that the patient's advance directives are documented and implemented**
  - **Discuss and document patient/family/caregiver wishes for resuscitation. In the event that CPR is unlikely to be effective, recommend other options such as DNR/DNAR/AND orders and promote comfort care.**
  - **Provide the patient/family/caregiver with respectful space and uninterrupted time together**
  - **Provide information on funeral planning, if desired**

See After-Death Interventions (PAL-34)

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PALLIATIVE SEDATION

- **Palliative sedation to unconsciousness, in which the intended effect is deep sedation, remains controversial.[t]**

- **Refractory symptoms are symptoms that cannot be adequately managed despite comprehensive, interdisciplinary palliative care that does not compromise consciousness.**

- **Confirm that the patient has refractory symptoms and is imminently dying.**
  - **Imminently dying patients have a prognosis of hours to days. If palliative sedation is being considered, prognosis should be 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.**
  - **Discontinuation of life-prolonging therapies (eg, artificial hydration/nutrition and/or withholding of cardiopulmonary resuscitation) often accompanies palliative sedation.**

- **Support 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 on the patient's response to recent and current medications.[h]**
  Typical sedatives used for palliative sedation parenteral infusions include:
  - **Midazolam**
  - **Propofol**

- **Continue current pain and symptom management interventions and titrate as needed.**

- **Monitor patient symptoms regularly, titrate sedatives and other medications, and reassess the need for ongoing palliative sedation 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.**

[h] See Drug Appendix (PAL-A) for specific recommendations for medical management of symptoms.

[t] Ten Have H, Welie JV. Palliative sedation versus euthanasia: an ethical assessment. J Pain Symptom Manage 2014;47(1):123-136. https://www.ncbi.nlm.nih.gov/pubmed/23742736.

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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	→ **For family and caregiver(s)** • Immediate after-death care: ▸ Inform family (if not present) of death ▸ Offer condolences ▸ Provide the family time with the body ▸ Involve chaplain to assess family's desire for religious ritual or spiritual support ▸ Remove tubes, drains, lines, and the foley catheter unless an autopsy is planned ▸ 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 and family as appropriate ▸ Inform other involved health care professionals 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 • Identify family members at risk for persistent complex bereavement disorder[g] **For health care professionals** • 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 ◊ Identify health care professionals at risk for persistent complex bereavement disorder,[g] moral distress, or compassion fatigue ◊ 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)

[g]Persistent complex bereavement disorder is a chronic heightened state of mourning that significantly impairs functioning.

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PALLIATIVE CARE DRUG APPENDIX

Condition	Recommended Agents and Dosage by Estimated Life Expectancy and Symptom Etiology
Dyspnea (PAL-11)	Life Expectancy: Years; Year to Months; and Months to Weeks • General: Morphine, 2.5–10 mg PO q2h PRN or 1–3 mg IV q2h PRN for opioid naïve, increase dose by 25% for non-opioid naïve ▸ For acute progressive dyspnea, or for patients who are not opioid naïve, more aggressive titration may be required • Anxiety: Lorazepam, 0.25–1 mg PO q4h PRN for benzodiazepine naïve
Dyspnea (PAL-12)	Life Expectancy: Weeks to Days (dying patient) • General: Morphine, 2.5–10 mg PO q2h PRN or 1–3 mg IV q2h PRN if opioid naïve, increase dose by 25% for non-opioid naïve ▸ For acute progressive dyspnea, or for patients who are not opioid naïve, more aggressive titration may be required • Anxiety: Lorazepam, 0.25–1 mg PO q4h PRN if benzodiazepine naïve • Fluid overload: Furosemide
Secretions (PAL-12)	• Excessive secretions: Scopolamine, 0.4 mg SC q4h PRN/1.5 mg patches, 1–3 patches q 72 h OR atropine, 1% ophthalmic solution 1–2 drops SL q4h PRN OR glycopyrrolate, 0.2–0.4 mg IV or SC q4h PRN
Anorexia/ Cachexia (PAL-13)	Life Expectancy: Years; Year to Months • Depression/anorexia: Mirtazapine, 7.5–30 mg PO QHS • Gastroparesis (early satiety): Metoclopramide 5–10 mg PO QID 30 min before meals and at bedtime • Low/no appetite: Megestrol acetate, 400–800 mg/d PO
Anorexia/ Cachexia (PAL-14)	Life Expectancy: Months to Weeks; Weeks to Days (dying patient) • Offer education to patient • Low/no appetite: Megestrol acetate, 400–800 mg/d PO OR olanzapine, 5 mg/d PO OR dexamethasone, 4–8 mg/d PO OR consider cannabinoid • Depression: Mirtazapine, 7.5–30 mg PO QHS

See key for abbreviations PAL-A (5 of 5)

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Continued

PALLIATIVE CARE DRUG APPENDIX

Condition	Recommended Agents and Dosage by Estimated Life Expectancy and Symptom Etiology
Nausea and Vomiting (NV)-Initial Treatment (PAL-15)	Life Expectancy: Years; Year to Months; Months to Weeks; and Weeks to Days (dying patient) • See NCCN Guidelines for Antiemesis for chemotherapy/radiation-induced NV • Gastroparesis: Metoclopramide, 5–10 mg PO QID 30 min before meals and at bedtime • CNS involvement: Dexamethasone, 4–8 mg PO BID-TID • Gastric outlet obstructions: Dexamethasone, 4–8 mg/d PO; proton pump inhibitor; metoclopramide, 5–10 mg PO QID 30 min before meals and at bedtime • Gastritis/GERD: Proton pump inhibitor OR H2 blocker • Medication-induced gastropathy: Proton pump inhibitor OR metoclopramide, 5–10 mg PO QID 30 min before meals and at bedtime Nonspecific NV • Dopamine receptor antagonists or 5HT3 receptor antagonists ‣ Haloperidol, 0.5 mg PO TID OR metoclopramide, 5–10 mg PO QID 30 min before meals and at bedtime OR prochlorperazine, 5–10 mg PO 3–4 times/d, maximum 40 mg/d OR olanzapine, 5–10 mg PO 2–3 times/d OR ondansetron, 4 mg PO q4h or 8 mg PO q8h • Contributing anxiety: Lorazepam, 0.5–1 mg PO q4h PRN • Vertiginous component: Anticholinergic AND/OR antihistamine
Nausea and Vomiting (NV)-Initial Treatment (PAL-16)	Life Expectancy: Years; Year to Months; Months to Weeks; and Weeks to Days (dying patient) • Consider appropriate route of administration ‣ 1) Prescribe oral, sublingual, or rectal agent and titrate to maximum benefit ‣ 2) If NV persists, provide PRN, scheduled, or continuous parenteral infusion as necessary ‣ 3) Consider subcutaneous administration as an alternative • Titrate to maximum benefit and tolerance: olanzapine, prochlorperazine, haloperidol, or metoclopramide • For continued NV, consider additional agents: ‣ Dexamethasone, 4–8 mg/d PO; ondansetron, 4–8 mg PO every 6 h; scopolamine (patch or IV); meclizine, 25–100 mg/d PO; oral cannabinoid
Constipation (PAL 17)	Life Expectancy: Years; Year to Months; Months to Weeks; and Weeks to Days (dying patient) • Prophylaxis: Titrate the senna and add polyethylene glycol, recommend starting with polyethylene glycol if the patient is not on opioids and can tolerate the volume of liquid • General: Add bisacodyl, titrate to 10–15 mg PO daily-TID with a goal of 1 non-forced bowel movement (BM) every 1–2 days • Persistent constipation: bisacodyl suppository, one rectally daily-BID; polyethylene glycol, 1 capful/8 oz water PO BID; lactulose, 30–60 mL PO BID-QID; sorbitol, 30 mL PO q2h x 3, then PRN; magnesium hydroxide, 30–60 mL PO daily-BID; or magnesium citrate, 8 oz PO daily • Opioid-induced constipation: Consider methylnaltrexone, 8 or 12 mg/dose SC, no more than once a day; linaclotide, 72–145 mcg/d PO; naloxegol, 12.5–25 mg/d PO ‣ Not for post-op ileus and mechanical bowel obstruction

See key for abbreviations PAL-A (5 of 5)

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Continued

PALLIATIVE CARE DRUG APPENDIX

Condition	Recommended Agents and Dosage by Estimated Life Expectancy and Symptom Etiology
Diarrhea (PAL-19)	Life Expectancy: Years; Year to Months; and Months to Weeks Grade 1 • General: Loperamide, 4 mg PO x 1 then 2 mg PO after each loose stool, up to 16 mg/d • If not on opioids: Diphenoxylate/atropine 1–2 tabs PO q6h PRN, maximum 8 tabs/d Grade 2 • Initiate/continue loperamide, 4 mg PO x 1 then 2 mg PO after each loose stool, up to 16 mg/d • If not on opioids: Diphenoxylate/atropine 1–2 tabs PO q6h PRN, maximum 8 tabs/d • Consider hyoscyamine, 0.125 mg PO/ODT/SL q4h PRN, max: 1.5 mg/d; atropine 0.5–1 mg SC/IM/IV/SL q 4–6h PRN • C. diff-induced: Metronidazole, 500 mg PO/IV QID x 10–14 days; vancomycin, 125–500 mg PO QID x 10–14 days • Non-C. diff infection: Treat appropriately based on culture findings • Immunotherapy-related: Dexamethasone, 4–8 mg/d; infliximab, 5 mg/kg q 2–6 weeks Grades 3/4 (Inpatient hospitalization w/ICU for Grade 4) • Initiate/continue loperamide, 4 mg PO x 1 then 2 mg PO after each loose stool, up to 16 mg/d • If not on opioids: Diphenoxylate/atropine, 1–2 tabs PO q6h PRN, maximum 8 tabs/d • Consider hyoscyamine, 0.125 mg PO/ODT/SL q4h PRN, max: 1.5 mg/d; atropine 0.5–1 mg SC/IM/IV/SL q 4–6 h PRN • Consider octreotide, 100–200 mcg/d SC, q8h or by continuous infusion
Diarrhea (PAL-19)	Life Expectancy: Weeks to Days (dying patient) • Reevaluate ongoing antidiarrheal, anticholinergic agents • Initiate or increase dose of around-the-clock opioid • Atropine 0.5–1 mg SC/IV/SL q 4–6h PRN • Consider octreotide, 100–200 microgram SC q8h • Consider glycopyrrolate, 0.2–0.4 mg IV q4h PRN
Malignant Bowel Obstruction (PAL-20)	Life Expectancy: Years; Year to Months; Months to Weeks; and Weeks to Days (dying patient) Goal to Maintain Gut Function • Reduce opioid dose or rotate opioid • Metoclopramide, 5–10 mg PO QID 30 min before meals and at bedtime • Dexamethasone, 4–12 mg IV daily, discontinue if no improvement in 3–5 days Gut Function Cannot be Maintained • Scopolamine (patch or IV); hyoscyamine, 0.125 mg PO/ODT/SL q4h PRN; glycopyrrolate, 0.2–0.4 mg IV q4h PRN • Octreotide, 100–300 mcg SC BID-TID or 10–40 mcg/h continuous SC/IV infusion; if prognosis >8 weeks, consider long-acting release (LAR) or depot injection

See key for abbreviations PAL-A (5 of 5)

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Continued

PALLIATIVE CARE DRUG APPENDIX

Condition	Recommended Agents and Dosage by Estimated Life Expectancy and Symptom Etiology
Sleep/Wake Disturbance (PAL-22)	Life Expectancy: Years; Year to Months; and Months to Weeks Insomnia • Trazodone, 25–100 mg PO at bedtime • Olanzapine, 2.5–5 mg PO at bedtime • Zolpidem, 5 mg PO at bedtime • Mirtazapine, 7.5–30 mg PO at bedtime • Chlorpromazine, 25–50 mg PO at bedtime • Quetiapine, 12.5–25 mg PO at bedtime • Lorazepam, 0.5–1 mg PO at bedtime • For phase shift disorder consider ramelteon (8 mg PO 30 min before bedtime) or melatonin (30 min before bedtime; dosage may vary by formulation) Daytime Sedation • Caffeine, 100–200 mg PO q 6 h, last dose 4 PM • Methylphenidate, start with 2.5–20 mg PO BID, second dose no later than 6 h before bedtime • Dextroamphetamine, 2.5–10 mg PO BID, second dose no later than 12 h before bedtime • Modafinil, 100–400 mg PO each morning Restless Legs Syndrome • Ropinirole, 0.25 mg PO 1–3 h before bedtime • Pramipexole, starting dose 0.125 mg PO at bedtime, may require titration • May also consider pregabalin, carbidopa-levodopa, or low-dose methadone with dopamine agonist; however, all of these medications are off-label for RLS
Sleep/Wake Disturbance (PAL-22)	Life expectancy: Weeks to Days (dying patient) • Titrate dose of existing pharmacotherapy • Consider chlorpromazine, 25–100 mg PO/PR at bedtime

See key for abbreviations PAL-A (5 of 5)

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Continued

PALLIATIVE CARE DRUG APPENDIX

Condition	Recommended Agents and Dosage by Estimated Life Expectancy and Symptom Etiology
Delirium (PAL-23)	Life Expectancy: Years; Year to Months; and Months to Weeks Mild/Moderate Delirium • Haloperidol, 0.5–2 mg PO BID/TID • Alternatives: risperidone, 0.5–1 mg PO BID; olanzapine, 5–20 mg PO daily; or quetiapine fumarate, 25–200 mg PO/SL BID Severe Delirium (agitation) • Haloperidol, 0.5–2 mg IV q1–4h PRN • Alternatives: olanzapine, 2.5–7.5 mg PO/SL q2–4h PRN (maximum = 30 mg/d); chlorpromazine, 25–100 mg PO/PR/IV q4h PRN for bedbound patients • High-dose neuroleptic-refractory: Consider adding lorazepam, 0.5–2 mg SC/IV q4h
Delirium (PAL-24)	Life Expectancy: Weeks to Days (dying patient) • Upward titrate haloperidol, risperidone, olanzapine • High-dose neuroleptic-refractory: Upward titrate lorazepam • Consider rectal or IV haloperidol • Consider chlorpromazine, 25–100 mg PO/PR at bedtime with or without lorazepam, 0.5–2 mg SC/IV q4h
Palliative Sedation (PAL-33)	Imminently dying patient • Midazolam, continuous infusion • Propofol, continuous infusion

Abbreviations Key

Timing: q (every); h (hour); d (day); BID (twice a day); TID (three times per day); QID (four times per day); QHS (at bedtime); PRN (as needed)
Route of administration: IM (intramuscular); IV (intravenous); ODT (orally disintegrating tablet); PO (oral); PR (rectal); SC (subcutaneous); SL (sublingual)

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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 indicated.

Table of Contents

Overview

The aim of the NCCN Guidelines for Palliative Care is to help assure that each patient with cancer experiences the best quality of life possible throughout the illness trajectory by providing guidance for the primary oncology team. The NCCN Palliative Care Panel is an interprofessional group of representatives from NCCN Member Institutions, consisting of medical oncologists, hematologists and hematologic oncologists, pediatric 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 are updated annually by the collaborative efforts of these experts based on their clinical experience and available scientific evidence.

More than 1.76 million people are expected to be diagnosed with cancer in the United States in 2019, and 606,880 people are expected to die of the disease.[1] Global cancer rates are increasing, with an associated rise in the number of cancer survivors living with symptoms and disabilities as a result of their disease and/or its treatment (see the NCCN Guidelines for Survivorship).[2-4] More than one-third of patients with cancer 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.[5] Greater access to palliative care may help to address the challenges faced by oncology patients and their families.

The Center to Advance Palliative Care (CAPC; www.capc.org) describes an optimal approach in which care is “provided by a team of palliative care doctors, nurses, and other specialists who work together with a patient’s other doctors to provide an extra layer of support. It is appropriate at any age and at any stage in a serious illness and can be provided along with curative treatment”.[6] During the past 20 years, increasing attention has been paid to quality-of life issues in oncology throughout the disease trajectory.[3,7-12] Palliative care in oncology began as hospice and end-of-life care, but it has developed into an integral part of comprehensive cancer care with the goal of early intervention to improve patient outcomes.

Literature Search Criteria and Guidelines Update Methodology

Prior to the update of this version of the NCCN Guidelines® for Palliative Care, an electronic search of the PubMed database was performed to obtain key literature in palliative care, using the following search terms: (palliative care AND cancer) OR (palliative care AND oncology) OR (hospice AND cancer) OR (hospice AND oncology) OR (“end of life” AND cancer) OR (“end of life” AND oncology). The PubMed database was chosen as it remains the most widely used resource for medical literature and indexes peer-reviewed biomedical literature.

The search results were narrowed by selecting studies in humans published in English. Results were confined to the following article types: Clinical Trial, Guideline, Meta-Analysis, Multicenter Study, Observational Study, Randomized Controlled Trial, Systematic Reviews, and Validation Studies.

The PubMed search resulted in 245 citations and their potential relevance was examined. The data from key PubMed articles selected by the panel for review during the Guidelines update meeting as well as articles from additional sources deemed as relevant to these Guidelines and discussed by the panel have been included in this version of the Discussion section (eg, e-publications ahead of print, meeting abstracts). Recommendations for which high-level evidence is lacking are based on the panel’s review of lower-level evidence and expert opinion.

The complete details of the Development and Update of the NCCN Guidelines are available at www.NCCN.org.

Palliative Care in Oncology

These guidelines define palliative care as an approach to patient/family/caregiver-centered health care that focuses on optimal management of distressing symptoms, while incorporating psychosocial and spiritual care according to patient/family/caregiver needs, values, beliefs, and cultures. The goal of palliative care is to anticipate, prevent, and reduce suffering and to support the best possible quality of life for patients/families/caregivers, regardless of the stage of the disease or the need for other therapies. Palliative care can begin at diagnosis and should be delivered concurrently with disease-directed, life-prolonging therapies and should facilitate patient autonomy, access to information, and choice. While palliative care previously focused on end-of-life care, the idea that palliative care needs to be integrated earlier into the continuum of cancer care is increasingly understood.[13-17] 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 (including physicians, nurses, social workers, mental health professionals, chaplains, advanced practice providers, pharmacists, and dietitians) and then augmented by collaboration with an interprofessional team of palliative care experts to address intractable symptoms and/or complex psychosocial issues. Additionally, palliative care efforts should reach beyond the patient to family and caregivers. When further anti-cancer therapy is likely to do more harm than good, palliative care becomes the predominant care offered to patients with advanced cancer. When this point in the disease trajectory is reached, palliative care can facilitate transfer to hospice care at home or in a care facility. For patients too unstable for transfer out of the inpatient setting, palliative care and/or hospice may provide end-of-life care for patients in the hospital. Palliative care should continue even after the patient's death in the form of bereavement support for the patient's family and caretakers.

The American Academy of Hospice and Palliative Medicine (AAHPM, www.aahpm.org), founded in 1988, and the CAPC (www.capc.org), established in 1999, are organizations dedicated to advancing the discipline of hospice and palliative medicine. These organizations seek to expand access to quality palliative care services for people with advanced illness in all settings. Multiple groups have described their ideas and approaches for, experience and outcomes with, and barriers to developing successful programs that integrate palliative care into routine oncologic care.[16-31]

Impact of Palliative Care

Studies have shown that integration of palliative care into the cancer care continuum, particularly early in the course of care, results in improved patient outcomes across multiple measures, including survival, quality of life, symptom intensity, and end-of-life care.

Survival

Several groups have investigated the potential survival benefit of palliative care for patients with cancer. A remarkable study showed that early introduction of palliative care does not only improve quality of life for patients with advanced cancer but can also improve survival.[32] Early palliative care consultation was a positive prognostic factor for overall survival among patients who were discontinuing anticancer therapy when compared with traditional care models.[33] Similarly, a retrospective analysis of 609 patients with terminal cancer suggested that increased duration of palliative care services was positively correlated with survival time.[34] In another study, home-based palliative care was associated with an equal or longer survival compared to inpatient palliative care in patients with cancer.[35]

Results were reported from the ENABLE III trial, which examined outcomes after early versus delayed initiation of palliative care in patients

with advanced cancer. Patients in the early palliative care group had significantly higher Kaplan-Meier 1-year survival rates than the delayed palliative care group (63% vs. 48%, *P* = *.038*).[36] The timing of interventions for caregivers was also examined in this trial, suggesting that earlier provision of palliative care for caregivers lessened their depression and stress burden scores.[37]

Symptom Intensity and Quality of Life

Palliative care has been shown to have a positive impact on quality of life while reducing symptom intensity, particularly when integrated early in the course of cancer care. In a systematic review and meta-analysis of 10 randomized controlled trials, patients with advanced illness who received specialist palliative care early, particularly those with advanced cancer (n = 1766/2454), had the most pronounced effects on quality of life.[38] A Cochrane database review of seven randomized and cluster-randomized controlled trials in patients with advanced cancer (n = 1614) compared early palliative care to treatment as usual/standard of care. Early palliative care significantly improved health-related quality of life and suggested lower symptom intensity compared with controls.[39,40] Another study demonstrated significant improvement in multiple symptoms within one day of a palliative care consultation, highlighting the potential benefit of palliative care even during brief hospital stays.[41]

In addition to quality of life, psychosocial factors have also been studied. Early integration of palliative care for newly diagnosed lung and gastrointestinal cancers was assessed by studying change in quality-of-life measures between baseline, week 12, and week 24. Improvements in quality of life and depression were observed for the lung cancer cohort at 12 and 24 weeks, with improved quality of life and mood reported in the gastric cancer cohort by week 12.[42] Compared with a care model in which palliative care was provided on an as-needed basis, standardized early palliative care referral also increased satisfaction with care among caregivers of patients with advanced cancer.[43]

End-of-Life Care

Various studies have evaluated the impact of palliative care on end-of-life care, specifically aggressive anticancer therapy near the end of life. A retrospective analysis of patients with advanced cancer highlighted the importance of early palliative care consultations (>3 months before death) and revealed an association between outpatient palliative care and decreased aggressiveness of end-of-life care.[44] Several studies have shown that palliative care reduces chemotherapy provided at the end of life. A population study conducted in Japan (n = 26,012) showed that palliative care consultation reduced the percentage of patients receiving inpatient chemotherapy use during the last 2 weeks of life.[45] In one trial, patients receiving early palliative care were less likely to receive intravenous chemotherapy in the last 60 days of life (odds ratio, 0.47; 95% CI, 0.23–0.99; *P* = .05),[46] likely because these patients had a more accurate understanding of their prognosis, which impacted decisions about their care.[47] A prospective study showed that early integration of palliative care facilitated the discontinuation of anticancer regimens and improved measures of quality of life for patients with advanced breast or gynecologic cancers.[33] Likewise, the lack of palliative care team consultation has been shown to be a predisposing factor for futile life-sustaining treatments at the end of life.[48] An observational study suggested that inpatient palliative care led to stabilized end-of-life care trajectories after discharge.[49]

Studies have also demonstrated that community-based or home-based palliative care services can positively influence patient care. These services have been associated with reduced need for end-of-life emergency department visits, reduced length and frequency of hospitalization, as well as fewer intensive care unit (ICU) admissions and

in-hospital deaths.[50-54] Palliative care has been shown to reduce symptom burden, improve quality of life, and increase the odds of dying at home. Similarly, a 2013 Cochrane Database systematic review that analyzed home palliative care in patients with advanced illness demonstrated reliable reduction of symptom burden and increased likelihood of dying at home without a negative impact on caregiver grief.[55]

Specialty Palliative Care

Systematic review of the palliative care in oncology data supported best outcomes with care provided by an interprofessional palliative care team initiated within eight weeks of diagnosis.[56] In much of the existing trial data, oncologist-alone care serves as the usual care arm, while interprofessional palliative care is provided in the intervention arm. The data strongly suggest that using an interprofessional team approach to provide oncologic and palliative aspects of care is superior to placing the entire burden on the oncologist alone. The principal investigators of several of these major trials support implementation of the TEAM approach (***T****ime*, an extra hour a month; ***E****ducation*, especially about prognostic awareness, achievable goals, and advance care planning; ***A****ssessments* done formally for symptoms, spiritual needs, and distress/coping; and ***M****anagement*, by an interprofessional team) as a structured way for oncology offices to design their care.[57]

A meta-analysis of trial data comparing outpatient specialty palliative care with usual care in adults with advanced cancer revealed a 14% increase in 1-year survival compared with controls (n = 646; 56% vs. 42%, *P* < .001) and a median overall survival benefit of 4.56 months. Quality of life was also significantly improved.[58] Specialist palliative care has also been linked to cost savings as well. Earlier palliative care consultations have been associated with decreased health care costs for patients with advanced cancer, including those with multiple comorbidities.[59,60] According to recent data, dedicated palliative care units and programs can be cost-effective and favorably impact health systems finances.[61,62]

Role of Hospice Care

Hospice is the most established model of palliative care for patients with a prognosis of less than 6 months and is eligible for coverage by third-party payers and Medicare. Enrollment in hospice has been shown to reduce hospitalization and receipt of high-intensity non-hospice care at the end of life. End-of-life care can often be more aggressive than what is supported by current evidence. Generally, Medicare patients with poor-prognosis cancer received highly intensive end-of life-care.[63] Furthermore, administration of chemotherapy late in the course of cancer care, including in the last days of life, is growing more common,[64,65] and oncologists have reported that they have found hospice regulations and reimbursement limitations too restrictive.[66] Overall, provision of end-of-life care was inconsistent and varied widely across regions, even among comprehensive cancer centers.[63,67]

An 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.[68] Moreover, a study of 207 deceased patients with cancer who had stopped cancer treatment showed reduced emergency department visits, hospitalizations, and other noncancer clinic visits for those enrolled in hospice.[69] Additionally, analyses of data from 3069 deceased patients more than 50 years of age (extracted from the Health and Retirement Study) revealed that hospice enrollment significantly decreased hospitalization, non-hospice health care utilization, and cost of care.[70]

Unfortunately, many studies have suggested that palliative and hospice care often go underutilized.[71-78] A recent analysis of SEER/Medicare care on hospice use in end-of-life cancer care (n = 55,058), found that hospice

enrollment ranged from about 51% for colorectal cancers up to 62% for prostate cancers.[71] Despite the 6-month prognosis eligibility, the median length of hospice service (LOS) for Medicare patients with cancer in 2016 was 19 days.[79] Approximately 28% of hospice patients died or were discharged within 7 days of admission to hospice care.[79] Thus, barriers to early referrals still exist.[17,75] Additionally, one study at an academic medical center revealed marked and unwarranted variation in hospice LOS within divisions and by doctors. For instance, in thoracic oncology, several oncologists had an average LOS of 36 days while others were clustered around 4 days for the same patient population. However, oncologists were receptive to feedback and training[80] By establishing hospice referrals as a quality improvement measure, one health system reported that median LOS in hospice doubled within a year of implementation.[81] Similarly, another recent study revealed that educational outreach and implementation of specific triggers for palliative care consultation were associated with increased hospice referrals and LOS.[82]

Training in Palliative Care

All health care professionals and trainees should participate in education that results in acquisition of palliative care knowledge, skills, and attitudes. The establishment of hospice and palliative medicine as a medical subspecialty in 2008 received support from at least 10 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.

Researchers at a large urban teaching hospital demonstrated the effectiveness of education on palliative care and referral criteria for increasing overall referrals to palliative care services and enhanced referrals for the purpose of pain management.[83] Effective training in palliative care can also positively impact provider, patient, and caregiver quality of life. One study suggested that an online palliative care education intervention for primary care physicians led to measurable improvements in patient outcomes such as pain, symptoms, and quality of life.[84] In a survey study, oncology fellows reported that training on end-of-life issues and goal-of-care discussions mitigated burnout and distress.[85]

Provider education and training in palliative care can positively impact providers and patients. The OPTIM (Outreach Palliative Care Trial of Integrated Regional Model) study is a multiregional, mixed-methods study that examined the effects of a palliative care intervention implemented across 4 regions of Japan.[86] The intervention consisted of provider education and training; education and awareness initiatives for the general public/patients; establishment of community-based palliative care teams to instruct community health care institutions; and establishment of regional palliative care centers to coordinate multidisciplinary community resources. Surveys were provided to patients, bereaved family members, physicians, and nurses both before and after the intervention. The results indicated an increased percentage of patients receiving palliative care and dying at home, increased patient- and family-reported quality of care, and decreased physician- and nurse-reported difficulties in providing palliative care.

Palliative care resources that may be useful for clinicians are listed in Table 1, below.

Communication in Palliative Care

A National Academy of Medicine report, *Communicating with Patients on Health Care Evidence*, found that 90% of Americans surveyed want to

know their options for tests and treatments and to be involved in decision-making for their health, with almost 50% wanting to discuss the option of forgoing anticancer therapy and continuing non-chemotherapy palliative care.[87,88] However, the report also found that few respondents had such discussions with their physicians.

Clinicians should discuss prognosis with patients and their families clearly and consistently to help them develop realistic expectations. Research suggests that the majority of patients queried express a desire to receive detailed prognostic information about their disease.[89-92] Assessment and confirmation of understanding of prognosis is important and may guide treatment decisions. In addition, determining the decision-making styles of patients and their families helps facilitate congruence of a patient's goals, values, and expectations with those of the family/caregiver(s). Clinicians should also determine the patient's assessment of the relative importance of quality of life compared with length of life. 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; misunderstanding a disease progression timeline can impair advance care planning, including discussions of preferences for cardiopulmonary resuscitation and other life-extending measures.[93]

Patients nearing the end of life should be assisted in reviewing and revising their life priorities, resolving unfinished business, and putting financial and personal affairs in order. 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 should be anticipated and carefully managed.[94-96] Finally, social and spiritual support, as well as careful resource management 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.

Communication Skills Training

Provider communication skills play a particularly important role for palliative care in oncology. However, several studies have revealed gaps in patient-centered communication with regard to patient prognosis and understanding of the intent of treatment. Valuable insight has been garnered regarding provider communication and patient understanding from the Cancer Care Outcomes Research and Surveillance (CanCORS) study of approximately 10,000 patients with lung or colorectal cancer. A survey of 1193 patients from CanCORS found that 69% of patients with advanced lung cancer and 81% of those with advanced colorectal cancer thought that their palliative chemotherapy could cure them.[97] It is unclear whether these patients were not told their prognosis, did not or could not understand the information, or merely disagreed with the information and answered the survey with a high degree of optimism.[98] This result, however, demonstrates a clear need for improvement in the area of physician-patient communication. Additional analyses of 722 patients with stage IV lung or colorectal cancer showed that only 33% of patients recognized that their chemotherapy regimens were "not at all" likely to cure their cancer.[99] Similar misconceptions also apply to palliative radiation therapy. In a study of 384 patients with inoperable lung cancer, 64% of patients did not understand that their radiation therapy was not curative.[100] Notably, in a cohort of 686 patients with metastatic lung or colorectal cancer from CanCORS, only 16.5% were able accurately to state their prognosis.[101]

Survey and observational data have revealed that many doctors are hesitant to have honest discussions with their patients, in part because these discussions can be very difficult and emotionally draining for the physicians.[102-104] Oncologists revealed a high level of perceived burden regarding discussions about discontinuing anticancer treatments, and study results have indicated a desire on the part of providers for additional communication skills training.[103,104] Training in communication has been shown to improve clinician-patient communication [105-109] and to mitigate physician burnout and improve physician empathy and mood.[110] For example, a recent randomized controlled trial showed that an 11-hour communication skills training workshop for oncologists was effective at improving communication skills, including those specific to the transition to palliative care.[111] Additionally, the VOICE cluster randomized controlled trial recently demonstrated the effectiveness of patient-centered communication training for physicians caring for patients with advanced cancer.[109]

Clear, consistent, and empathetic communication with the patient, family, and caregiver(s) about the natural history of the cancer and its prognosis is at the core of effective palliative care.[112-116] It is important to assess and reassess patient goals and preferences regarding communication of difficult news over the course of disease.[117] When patients understand the goals of treatment, they can make choices that are consistent with their life goals. A multicenter observational study revealed that prognostic disclosure from physicians resulted in more realistic patient expectations regarding life expectancy without reducing emotional well-being or patient ratings of their physician relationship.[118] In addition, effective patient-physician communication has been shown to decrease patient stress, increase adherence to treatment, and improve outcomes.[119,120] Open communication with relatives or caregivers of patients with cancer is also critical, particularly when patients near the end of life.[115,121]

Based on existing evidence and expert consensus, ASCO released a consensus guideline in 2017 addressing how to improve patient-clinician communication on topics such as goals of care, prognosis, end-of-life care, and facilitating family involvement in care.[122]

NCCN Guidelines for Palliative Care

The NCCN Guidelines for Palliative Care 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 initially focused on the needs of patients in their last 12 months of life in order to distill the content of textbooks and curricula into guidelines in a manner similar to existing NCCN disease-oriented and symptom-oriented guidelines. The Palliative Care Guidelines have expanded the focus to all patients and family experiencing cancer throughout the disease trajectory, consistent with the Provisional Clinical Opinion from ASCO.[123]

Screening

The primary oncology team should screen all patients at every visit for one of more of the following: 1) unmanaged symptoms; 2) moderate to severe distress related to cancer diagnosis and therapy; 3) serious comorbid physical and psychosocial conditions; 4) complex psychosocial needs; 5) poor prognostic awareness; 6) potentially life-limiting disease; 7) metastatic solid tumors or refractory hematologic malignancies; 8) patient/family/caregiver concerns about the course of disease and decision-making; 9) patient or family requests for palliative care; and/or 10) patient request for hastened death. Patients who meet these screening criteria[124] and those who make a specific request for palliative care 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,

family, and caregivers about palliative care services. Anticipation of palliative care needs and prevention of symptoms should be discussed, and conversations regarding advance care planning should be initiated.

Comprehensive Assessment

Patients who meet screening criteria (see above) should undergo a comprehensive palliative care assessment by their primary oncology team evaluating the benefits and burdens of anticancer therapy; physical symptoms; psychosocial or spiritual distress; personal goals, values, and expectations; educational and informational needs; and cultural factors affecting care.[7-9]

Assessment for Benefits and Burdens of Anticancer Therapy

Many cancer symptoms can be relieved by control of the cancer with anti-cancer therapy. Assessment of the benefits and burdens of anticancer therapy for each individual is based on the existing NCCN disease-specific guidelines (the most recent version of all guidelines can be found on the NCCN website 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 the patient/family/caregiver(s); 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.

Assessment of Patient/Family/Caregiver Goals, Values, Expectations, and Priorities

Patients and their families should also be asked about their personal goals, values, expectations, and priorities. Shared decision-making with patient, family, and caregiver(s) is important. A 2015 systematic review of quantitative studies identified the following elements of palliative care that were ranked as most important by patients and their families: effective communication and shared decision-making; expert care; respectful and compassionate care; and trust and confidence in clinicians.[116]

Patients' priorities should be discussed, including their goals, their definition of quality of life, and their perception of how anticancer therapy will fit into their lives. Survival statistics may be helpful in these conversations; however, patients' abilities to assimilate such data should be assessed. Goals and expectations that might be better met by the hospice model of palliative care should be identified. Patients should be given the opportunity to understand the expected trajectory of their disease, particularly if it is incurable.

Assessment of Physical Symptoms

The most common symptoms are pain, dyspnea, anorexia, cachexia, nausea, vomiting, constipation, malignant bowel obstruction (MBO), fatigue, weakness, asthenia, insomnia, daytime sedation, and delirium.[125] Palliative interventions for these symptoms are discussed individually below.

Assessment of Psychosocial Distress

Assessment of psychosocial distress should focus on illness-related distress and psychosocial, spiritual, or existential needs according to the NCCN Guidelines for Distress Management. Concerns regarding 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 below and in the NCCN Guidelines for Distress Management.

Assessment of Educational and Informational 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/caregiver regarding the patient's disease status.[95,126]

Criteria for 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 for patients with a life-limiting cancer diagnosis or limited anticancer treatment options due to lack of access to anticancer therapy; advanced disease process; multiple/severe comorbid conditions; rapidly progressive functional decline; and/or persistently poor performance status. Additional criteria include high risk for poor pain management; high burden of non-pain symptoms resistant to conventional management; frequent emergency department visits or hospital admissions; need for ICU-level care; need for invasive procedures (eg, palliative stenting/gastrostomy); or a high distress score (eg, ≥4 on the Distress Thermometer; see the NCCN Guidelines for Distress Management). Consultation with palliative care specialists should also be considered when there is a need for clarification of the goals of care; patient/family/caregiver or provider dissatisfaction with the care plan; resistance to advance care planning; or a request for hastened death.

Difficult social circumstances or a high risk for persistent complicated bereavement disorder indicate a need for referral for consultation with a palliative care specialist. These may include family/caregiver limitations, inadequate social support, substance abuse, 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, unresolved or multiple prior losses, and/or dependent children and/or older relatives living in the household.

Palliative care consultation should also be considered when complex care coordination issues exist within or among multiple care teams, or if staff issues such as compassion fatigue, moral distress, or burnout are present. For more information regarding psychosocial issues affecting care providers, see the section on *Psychosocial Support for Palliative Care Providers*.

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 concerns to improve their quality of life and survival.[32,35,36,123] Referrals should be made as needed to mental health and social services, pastoral care, health care interpreters, hospice services, or other specialists. Finally, the oncology team may be helpful in identifying additional support through religious organizations, schools, or other agencies in the community.

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, values, 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, caregiver(s), 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), persistent hypercalcemia, central nervous system metastases, delirium, MBO, superior vena cava (SVC) syndrome, spinal cord compression, cachexia, malignant effusions, need for palliative stenting or venting gastronomy, potentially life-limiting disease, or other serious comorbid conditions. Many patients with stage IV cancers, especially those with metastatic lung cancer, pancreatic cancer, and glioblastoma multiforme, would benefit from palliative care beginning at diagnosis, because expected survival is limited.[127-129] Palliative care interventions for managing specific symptoms and the benefits and burdens of anticancer therapy are discussed below as outlined in the algorithm. 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.[130-133] Anticancer therapy may be conventional evidence-based treatment as outlined in the NCCN disease-specific guidelines (available 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.[134,135] Palliative RT also plays an important role in the management of patients with advanced cancer.[136-138]

Furthermore, patients with advanced cancer who are not eligible for systemic chemotherapy may benefit from immunotherapy or molecular targeted therapies that may be effective for relieving symptoms, maintaining stable disease, and/or improving quality of life without the adverse events that may be associated with cytotoxic cancer therapies.[139,140] Physicians, patients, and their families should discuss prognosis, intent and goals of therapy (palliative or curative), range of choices, benefits and burdens of anticancer therapy, and possible effects on quality of life. In addition, the oncology team should prepare the patient psychologically for possible disease progression or recurrence.

Provide primary palliative care to include both anticancer treatment aligned with patient goals and priorities and disease-related symptom management. Anticancer therapy should be in line with stated patient goals and priorities and be accompanied by appropriate prevention/management of side effects as well as palliative care. A recent longitudinal cohort study evaluated the impact of palliative chemotherapy on quality of life near death as a function of patient performance status. In patients with progressive metastatic cancer, palliative chemotherapy failed to improve quality of life near death for those with moderate or poor performance status and worsened quality of life near death for those with initially good performance status.[141] Studies have reported that, at times, anticancer therapy may go beyond what is evidence-based for patients with advanced or metastatic disease.[45,142,143]

Patients with months to weeks to live should be provided with guidance regarding the anticipated course of the disease. Physicians should confirm patients' understanding of goals of therapy and preferences regarding prognostic information. As functional status worsens, these patients may become more concerned about the side effects of cancer-directed treatment and consider focusing their care on maintaining quality of life. The option of discontinuing anticancer treatment not directly addressing a symptom complex and initiating goal-directed supportive care should be discussed, including referral to specialized palliative care services or hospice.[140,141,144-146] To avoid demeaning the value of end-of-life care,

palliative care and/or hospice care should not be described as “giving up,” but instead reframed as “fighting” for better quality of life.

In general, patients with weeks to days to live (ie, dying patients) should discontinue all treatments not directly contributing to patient comfort. Intensive palliative care focusing on symptom management should be provided in addition to preparation for the dying process. Refer to hospice when possible.

Symptom Management

Special considerations in the implementation of these guidelines based on life expectancy are delineated in the algorithm. The major focus of these special considerations is the withholding and withdrawal of aggressive interventions; prevention and elimination of side effects associated with pharmacologic 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 management of pain, dyspnea, anorexia/cachexia, nausea and vomiting, constipation, diarrhea, MBO, fatigue, delirium, and psychological distress is fundamental[147-149] and discussed in detail below. As a general principle, if/when appropriate, providers should try to use palliative interventions that may address multiple symptoms.

Pain

See the NCCN Guidelines for Adult Cancer Pain for specific recommendations for pain management and education on opioid safety. Provide education to the family/caregiver on the role of pain medications, customizing the education to the patient’s particular situation. 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 when opioid is necessary for adequate management of dyspnea and pain. In fact, opioids can be titrated aggressively for moderate/severe acute/chronic pain.[150] In addition, palliative sedation can be considered for refractory pain (see below) following consultation with pain management/palliative care specialists. Short-course palliative RT may be used to address pain associated with bone metastases.[137,138,151,152] Study data suggests that 40% of patients (122/298) who received a single 8 Gy RT dose for painful bone metastases experienced pain reduction and improved quality of life within 10 days.[152]

Dyspnea

Dyspnea is one of the most common symptoms in patients with advanced lung cancer.[153] 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.”[154] Symptoms should first be comprehensively assessed in all patients. In non-communicative patients with weeks to days to live, symptom intensity should be assessed using physical signs of dyspnea. Education should be provided to the patient/family/caregiver on the patient’s condition and the risk/benefit of treatment options. Potentially reversible underlying causes or comorbid conditions should be treated using chemotherapy or radiation therapy; therapeutic procedures for cardiac, pleural, or abdominal fluid[155-157]; bronchoscopic therapy; or bronchodilators, diuretics, steroids, antibiotics, transfusions, or anticoagulants for pulmonary emboli. Palliative RT can be considered for patients with SVC syndrome or those who have respiratory obstruction by tumor mass.[136,158]

Both pharmacologic and non-pharmacologic interventions have been investigated in the management of dyspnea. A review concluded that little definitive data evaluating the effectiveness of dyspnea interventions exist and that randomized controlled trials are needed.[159,160] Other reviews have determined that there are sufficient data to make treatment recommendations.[156,161] Recommended pharmacologic interventions

include opioids with or without benzodiazepines.[156,159,160,162-165] Benzodiazepines can be considered for coexisting anxiety. However, the reported beneficial effect of benzodiazepines on dyspnea in patients with advanced cancer is small, and the addition of benzodiazepines to opioids can increase the risk of respiratory depression.[159,166]

Of the opioids, morphine has undergone the most extensive investigation for treating dyspnea in patients with cancer; recent studies have also looked at opioids such as fentanyl and oxycodone. Prophylactic fentanyl provided through buccal or subcutaneous routes improved episodic, exertional dyspnea in two small randomized, controlled trials in patients with cancer.[167,168] Nebulized fentanyl has also been studied. A single-institution trial of nebulized fentanyl in patients with cancer with dyspnea showed improved oxygenation and reduced tachypnea, and 79% of patients said it improved their breathing.[169] An attempted randomized, placebo-controlled trial at the same institution was not successful, because the practice had already diffused widely with over 1000 doses being prescribed.[170] Additionally, an observational study of 136 patients with terminal cancer also suggested that continuous infusion of subcutaneous oxycodone may provide relief of dyspnea in addition to relief of pain.[171] For patients receiving chronic opioids, the panel recommends consideration of a 25% dose increase to manage dyspnea.

Scopolamine, atropine, hyoscyamine, and glycopyrrolate are options to reduce excessive secretions associated with dyspnea.[172-176] Glycopyrrolate does not effectively cross the blood–brain barrier and is less likely than the other drug options to cause delirium, but this agent can produce anticholinergic side effects.[177-179] Scopolamine can be administered subcutaneously or transdermally; physicians should be aware that the onset of benefit for transdermal scopolamine patches is about 12 hours,[180] and they thus may not be an appropriate choice for imminently dying patients. A subcutaneous injection of scopolamine can be administered when the patch is applied or if management of secretions is inadequate.

Non-pharmacologic interventions include the use of handheld fans directed at the face,[181,182] cooler temperatures, supplemental oxygen, and time-limited trials of noninvasive mechanical ventilation if indicated. A randomized controlled trial examined the effects of room air versus palliative oxygen delivered via nasal cannula in patients with refractory dyspnea. Dyspnea scores were no different among patients receiving palliative oxygen versus room air, encouraging the use of less burdensome interventions.[183]

High-flow nasal oxygen and noninvasive mechanical ventilation are not available outside of the hospital setting, but may provide temporary improvements in hypoxemia and dyspnea. In a recent feasibility study of 200 patients with solid tumors randomized to receive either noninvasive positive-pressure ventilation (biphasic positive airway pressure, BiPAP) or conventional oxygen therapy, patients in the ventilation group had greater improvements in dyspnea symptoms and required lower doses of opiates than patients in the oxygen group.[184] A smaller phase II randomized trial comparing high-flow oxygen to BiPAP for persistent dyspnea in patients with advanced cancer revealed no significant differences between the two approaches.[185]

When caring for actively dying patients, providers should discuss the reversibility of respiratory failure and treatment options, and provide anticipatory guidance for patient/family/caregiver(s) about dying of respiratory failure. As life expectancy decreases, the role of mechanical ventilation and oxygen diminishes, and the role of pharmacologic interventions such as opioids, benzodiazepines, glycopyrrolate, and scopolamine increases. If fluid overload is a contributing factor, enteral and parenteral fluids should be decreased or discontinued, and low-dose diuretics can be considered.

Anorexia/Cachexia

Cachexia is physical wasting with loss of skeletal and visceral muscle mass and is very common among patients with cancer.[186,187] 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.[186,187] 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, shorter survival, and psychosocial distress.[186-188] A recent study that examined cancer cachexia in a cohort of 1473 patients across all weight ranges showed that muscle depletion conveys a similarly poor prognosis as involuntary weight loss, regardless of body mass index.[189]

Initial steps include evaluating the rate and severity of weight loss and associated symptoms, and educating the patient/family/caregiver on the patient's condition and discussing the risk/benefit of available treatment options. Clinicians should address conditions or symptoms that interfere with food intake, such as mucositis, oropharyngeal candidiasis, depression, nausea and vomiting, and pain, among others, and psychiatric evaluation may be considered if the patient has a history of an eating disorder. Treatment may include the relief of symptoms that interfere with food intake (eg, pain, constipation, nausea/vomiting), as well as metoclopramide for early satiety due to gut dysmotility.[156,161,190]

For patients with months-to-weeks or weeks-to-days life expectancy, appetite stimulants may be helpful (eg, megestrol acetate, dexamethasone, olanzapine) if increased appetite is an important aspect of quality of life.[191-195] A recent systematic review and meta-analysis of megestrol acetate revealed improved appetite and slight improvements in weight gain when using this drug to treat anorexia/cachexia in patients with cancer.[192] While one quarter of patients treated with megestrol acetate may have increased appetite and 1 in 12 may improve their weight, clinicians should be mindful of the increased risks of thromboembolic phenomena and death.[192]

A combination therapy approach may yield the best possible outcomes for patients with cancer cachexia. A randomized phase III trial in 332 patients with cancer-related anorexia/cachexia revealed superior outcomes for patients receiving a combination regimen that included medroxyprogesterone, megestrol acetate, eicosapentaenoic acid and L-carnitine supplementation, and thalidomide, versus therapy with any of the above single agents.[196] Another phase III trial of 104 patients with advanced gynecologic cancers and cachexia supported the merits of combination therapy; compared with megestrol acetate alone, patients receiving megestrol acetate plus L-carnitine, celecoxib, and antioxidants had improved lean body mass, appetite, and quality of life.[197]

Although cannabinoid-based interventions (eg, dronabinol, cannabis) have some demonstrated efficacy for treating chemotherapy-induced nausea and vomiting and AIDS-related anorexia, the data to support cannabinoid-based interventions for treating anorexia/cachexia in patients with cancer are very limited, in part due to legal constraints within this field of research.[198] A randomized clinical trial of cannabis extract and delta-9-tetrahydrocannabinol in patients with cancer-related anorexia-cachexia syndrome did not demonstrate a benefit of these agents over placebo on appetite and quality of life.[199] Another randomized trial comparing megestrol acetate to dronabinol in treating cancer-associated anorexia revealed megestrol acetate to be superior for promoting weight gain (75% vs. 49% of patients) and appetite (11% vs. 3%) in patients with advanced cancer.[200] However, to a lesser extent, dronabinol did improve appetite and weight gain in some study patients. Ultimately, for some patients with

cancer-related anorexia, cannabinoids could be helpful. However, it is important to note that cannabinoid administration in elderly patients may induce delirium, and providers should be aware of the local state rules and regulations regarding medicinal cannabinoid use.

Although some studies show nutritional interventions to be ineffective,[201] nutrition consultation should be considered, because calorie-dense, high-protein supplementation has demonstrated some efficacy for weight stabilization.[156,186,202-204] A meta-analysis found that while nutritional intervention does not significantly affect weight gain or energy intake, it can improve some aspects of quality of life, including emotional functioning, dyspnea, and hunger.[205] Nutritional 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 and the patient's life expectancy is months to years.[206]

The goals and intensity of nutritional support change as life expectancy is reduced to weeks to days. Education and emotional support should be provided regarding the natural history of the disease, as nutritional support might not reverse weight loss in patients with advanced cancer. Overly aggressive enteral or parenteral nutrition therapies can actually increase the suffering of dying patients.[206-209] In addition, a recent randomized controlled trial of patients with cancer enrolled in hospice found that parenteral hydration had no effect on dehydration symptoms such as fatigue and hallucination, nor any effect on quality of life or survival.[210] Therefore, instead of artificial hydration and nutrition, palliative care in the final weeks of life focuses on treating dry mouth and thirst, and providing education and emotional support to the patient, family, and caregiver(s) regarding the emotional aspects of withdrawal of nutritional support.

Nausea and Vomiting

Chemotherapy-induced nausea and vomiting has a major impact on a patient's quality of life.[211] Nausea and vomiting induced by chemotherapy or radiation therapy should be managed as outlined in the NCCN Guidelines for Antiemesis. Patients can also experience nausea and vomiting unrelated to chemotherapy and radiation, resulting from gastric outlet obstruction, bowel obstruction, constipation, opioid use, or hypercalcemia.[212] These causes should be identified and treated. Palliative RT should be considered for nausea and vomiting related to brain metastases.[136,213,214] Proton pump inhibitors and histamine-2 (H2) receptor antagonists can be used to manage gastritis or gastroesophageal reflux. Gastric outlet obstruction may benefit from treatment with corticosteroids; alternative treatment options include endoscopic stenting or insertion of a decompressing G-tube. Many medications (including non-prescribed supplements and herbs) can also cause nausea and vomiting. Blood levels of possible culprits, such as digoxin, phenytoin, carbamazepine, and tricyclic antidepressants, should be checked.[215,216] Also, patients should be screened for excess use of marijuana/cannabis for possible cannabis-associated hyperemesis syndrome, and counseled regarding cessation if indicated.

Non-specific nausea and vomiting are often managed with dopamine– or 5-HT3 (5-hydroxytryptamine 3)–receptor antagonists (eg, prochlorperazine, haloperidol, metoclopramide, olanzapine, ondansetron). However, experts have debated the quality and strength of the evidence to support specific agents in the management of nonspecific nausea and vomiting in palliative care.[217,218] A systematic review assessed the level of evidence for antiemesis unrelated to chemotherapy, concluding that antiemetic recommendations have moderate to weak evidence at best; the strongest evidence supported the use of metoclopramide.[218] For anxiety-related nausea, the addition of benzodiazepines can be considered. If a vertiginous component to the nausea and vomiting exists, anticholinergic/antihistamine agents may be appropriate. Non-pharmacologic therapies such as acupuncture, hypnosis, and cognitive behavioral therapy (CBT) can also be considered.[219-221]

For persistent nausea and vomiting, the panel recommends titrating dopamine receptor antagonists to maximum benefit and tolerance.[222-226] In the setting of continued nausea and vomiting, consider additional drug classes with potential antiemetic properties: corticosteroids,[227-229] 5-HT3 receptor antagonists,[230-232] anticholinergic agents and/or antihistamines,[228] oral cannabinoids,[233,234] or the antidepressant mirtazapine. The appropriate route of administration should be considered; the panel recommends prescribing oral, sublingual, or rectal agent as appropriate and titrating to maximum benefit. Opioid rotation can also be considered. For persistent/refractory nausea and vomiting, parenteral infusions can be provided as needed/PRN, scheduled, or continuously. Subcutaneous administration of antiemetic agents can also be used as an alternative. An around-the-clock dosing schedule may provide the most consistent benefit to the patient. Continuous intravenous or subcutaneous infusions of different antiemetics may be necessary for the management of intractable nausea and vomiting.

Palliative sedation (see below) can be considered as a last resort if intensified efforts by specialized palliative care or hospice services fail.

Constipation

Constipation occurs in approximately 60% of patients with advanced cancer and most patients treated with opioids.[235,236] Although several drugs including antacids, anticholinergic drugs (antidepressants, antispasmodics, phenothiazines, and haloperidol), and antiemetics are known to cause constipation,[237] opioid analgesics are most commonly associated with constipation. In addition to physical discomfort, constipation in patients with advanced cancer can cause psychological distress and anxiety regarding continued opioid use.[238] Opioid-induced constipation (OIC) should be anticipated and treated prophylactically with a stimulant laxative with or without osmotic laxative.[239] Increasing intake of fluid and physical activity should also be encouraged, when appropriate. Added dietary fiber may be considered for patients with adequate fluid intake.

If constipation is present, the cause and severity should be assessed. Impaction, obstruction, and other treatable causes, such as hypercalcemia, hypokalemia, hypothyroidism, and diabetes mellitus, should be identified and treated. Providers should discontinue any nonessential constipating medications. Constipation may be treated by stimulant and/or osmotic laxative with a goal of one non-forced bowel movement every 1 to 2 days. If impaction is observed, glycerine suppositories (with or without mineral oil retention enema) may be administered or manual disimpaction may be performed. Suppositories and enemas should be used with caution in patients receiving chemotherapy due to the increased risk of the rectal route of administration in the setting of cytopenia. While there is limited evidence regarding the best initial bowel regimen in patients with cancer,[240] one small study compared the use of senna alone versus a senna-docusate combination. The results suggested that the addition of the stool softener docusate was not necessary.[241] 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.[240] If gastroparesis is suspected, the addition of a prokinetic agent, such as metoclopramide, may be considered.

Peripherally acting μ-opioid receptor antagonists may help to relieve OIC while maintaining pain management.[242] Recent studies have shown that methylnaltrexone provided effective relief of OIC while preserving opioid-mediated analgesia.[243,244] Naloxegol, a similar peripherally acting μ-opioid receptor antagonist, has also been studied for treating OIC in patients receiving chronic opioids for noncancer pain.[245,246] Based on these results, the NCCN 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 postoperative ileus or mechanical bowel obstruction. Gastrointestinal specialists have reported some success also using erythromycin for constipation symptoms that do not respond to peripherally acting μ-opioid receptor antagonists such as methylnaltrexone.

Several newer agents have also been examined for treating constipation. Lubiprostone is a prostaglandin analog oral medication that activates select chloride channels to enhance intestinal fluid secretion.[247,248] It has been shown to be effective for treating OIC in patients with chronic noncancer pain and can be used in combination with a peripherally acting μ-opioid receptor antagonist such as methylnaltrexone. Linaclotide is a selective agonist of guanylate cyclase-C receptors in the intestines that also enhances intestinal secretions, and has been effective in the treatment of constipation associated with irritable bowel syndrome and chronic idiopathic constipation.[249,250] The American Gastroenterological Association includes lubiprostone and linaclotide as recommended options for treating constipation associated with irritable bowel disorder.[251]

Diarrhea

In patients with cancer, diarrhea can be caused by a number of potential factors, including anticancer treatment-related side effects, infection, antibiotic use, dietary changes, or fecal impaction.[252] Diarrhea is a common side effect of various chemotherapeutics (eg, fluorouracil and irinotecan), as well tyrosine kinase inhibitors and certain biologic agents (eg, ipilimumab, cetuximab, panitumumab).[253-256] Abdominal and pelvic radiation therapy (alone or as part of chemoradiation regimens) can also induce gastrointestinal toxicity resulting in diarrhea.[254,255]

The National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) are typically used for measuring diarrhea in this patient population.[252] The panel recommends that patients be screened and assessed to determine the severity (grade) and cause of diarrhea. Providers should provide immediate intervention for dehydration based on grade and tailor treatment to potential causes.

For patients who have grade 1 or 2 diarrhea, recommendations include hydration and electrolyte replacement (oral or IV fluids as appropriate) and antidiarrheal medications (eg, diphenoxylate/atropine) if the patient is not already on opioids. If the diarrhea is thought to be chemotherapy-related, dose reduction or discontinuation of therapy may be appropriate. For grade 2 diarrhea, anticholinergic agents such as hyoscyamine or atropine can be considered in addition to the interventions recommended for grade 1. Infection-induced diarrhea should be treated with the appropriate antibiotic. Immunotherapy-related diarrhea can be treated with corticosteroids, infliximab, and/or probiotics (see the NCCN Guidelines for Management of Immunotherapy-Related Toxicity). Patients with grade 3 or 4 diarrhea should receive inpatient treatment (intensive care for Grade 4 diarrhea if consistent with patient goals). In addition to fluid replacement, antidiarrheal therapy, and anticholinergics, somatostatin analogs (eg, octreotide) can also be considered. For diarrhea due to graft-versus-host disease (GVHD), diet alterations including IV nutrition and steroids may be necessary. In the home setting, subcutaneous hydration can be considered.

For patients with weeks to days of estimated life expectancy, the above interventions can be considered if consistent with the goals of care. At-home IV hydration may be considered in addition to scopolamine or hyoscyamine. If diarrhea persists, consider octreotide or glycopyrrolate. Patients with pain should be started on around-the-clock opioids or receive an increased dose of ongoing opioid regimens.

Malignant Bowel Obstruction

Initial steps should include evaluating the severity and cause(s) of bowel obstruction and educating the patient, family, and caregiver(s) on the

patient's condition and available treatment options. Underlying causes that are potentially reversible as well as malignant causes should be identified and treated. MBOs are usually diagnosed clinically and confirmed with radiography. The choice of intervention should be guided by the goals of treatment, taking into account prognosis and relative invasiveness of the intervention proposed.

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, including risk of mortality, morbidity, and re-obstruction.[257] 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. Risk factors for poor surgical outcome include ascites, carcinomatosis, palpable intra-abdominal masses, multiple bowel obstructions, previous abdominal radiation, advanced disease, and poor overall clinical status.[258] In these patients, medical management can include pharmacologic measures, parenteral fluids, endoscopic management, and enteral tube drainage (silicone tubing may offer superior comfort over vinyl).

Pharmacologic management of malignant bowel obstruction can be separated into two groups of patients: those for whom the goal is to maintain gut function and those for whom gut function is no longer possible. When the goal is maintaining gut function, patients can be treated with opioids, antiemetics, and corticosteroids, alone or in combination. When gut function is no longer considered possible, pharmacologic options also include somatostatin analogs (eg, octreotide) and/or anticholinergics.[259-264] If octreotide is helpful and the patient has a life expectancy of at least 1 month, it may be beneficial to consider a depot form of octreotide once an optimal dose is established. 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. Use of octreotide is recommended early in the diagnosis because of its efficacy and tolerability.[265,266] Despite positive findings from several smaller randomized trials, a recent phase III trial of octreotide in 86 patients with MBO failed to demonstrate a significant effect of this drug on days free of vomiting, number of vomiting episodes, symptom management, and other secondary endpoints.[267]

A venting gastrostomy tube (inserted by interventional radiology, endoscopy, or surgery) or an endoscopically placed stent can also palliate symptoms of MBO.[268-272] Total parenteral nutrition can be considered to improve quality of life in patients with a life expectancy of years to months. These interventions have been shown to have little positive impact on survival time, but may improve quality of life.[127,128]

Fatigue/Weakness/Asthenia

The data on methylphenidate for treating cancer-related fatigue have been mixed.[273] While some trials have suggested a dose-dependent benefit of this agent on fatigue symptoms,[274,275] other studies have failed to produce positive results.[276] Phase III randomized trials of modafinil for treating cancer-related fatigue suggested that modafinil had a modest efficacy and was most effective for those with severe fatigue.[277,278] A recent Cochrane Database review summarized the existing data on psychosocial interventions for fatigue during palliative care for cancer.[279] For more information, see the NCCN Guidelines for Cancer-Related Fatigue.

Sleep/Wake Disturbances Including Insomnia and Sedation

Patients with cancer often suffer from insomnia or daytime sedation.[280-282] In a recent study of 442 patients with advanced cancer, 330 (75%) patients were assessed as having baseline sleep disturbance as assessed by the Edmonton Symptom Assessment System (ESAS) sleep item.[283]

The type and severity of sleep/wake disturbance should first be evaluated using, for example, the Epworth Sleepiness Scale.[284] 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, 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.[285,286] Primary sleep disorders, such as OSA and periodic limb movement disorder, should be treated with nocturnal continuous positive airway pressure (CPAP) or BiPAP.[287] Restless leg syndrome, if present, can be treated with ropinirole, pramipexole with pregabalin, or carbidopa-levodopa.[288-296] Fears and anxiety regarding death and disease should be explored, and other contributing factors to sleep/wake disturbances should be treated, including pain, depression, anxiety, delirium, and nausea. CBT may be effective in treating sleep/wake disturbances in patients with cancer.[161,297-301]

For refractory insomnia, recommended pharmacologic management options include the short-acting benzodiazepine lorazepam; the non-benzodiazepine zolpidem; antipsychotic medications such as chlorpromazine, quetiapine, and olanzapine; and sedating antidepressants such as trazodone and mirtazapine.[302] 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.[303] Caution should be exercised when administering zolpidem due to the known risk of next-morning impairment. In 2013, the U.S. Food and Drug Administration (FDA) required lower recommended doses of zolpidem (ie, from 10 mg to 5 mg for immediate-release products and from 12.5 mg to 6.25 mg for extended-release formulations).[304]

For refractory daytime sedation, the guidelines suggest several options. The central nervous system stimulants methylphenidate or dextroamphetamine should be given with a starting dose of 2.5 to 5 mg orally (PO) with breakfast. If the effect of the drug does not last through lunch, a second dose can be given at lunch, preferably no later than 2:00 PM. Doses can be escalated as needed.[305] Another option for refractory daytime sedation is the psychostimulant modafinil, which has been approved in adults for excessive sleepiness associated with OSA/hypopnea syndrome (OSAHS), shift work sleep disorder, and narcolepsy.[306] 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 4:00 PM.

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 Guidelines for Adult Cancer Pain and the NCCN Guidelines for Cancer-Related Fatigue for their discussions on sleep/wake disturbances.

Delirium

Delirium should be evaluated for severity and cause using the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria.[307] Potentially reversible causes should be identified and treated appropriately.[308] Delirium may present as either a hypoactive or a hyperactive subtype.[309] Recent studies have suggested that hypoactive delirium was the most prevalent subtype in palliative care patients and that this condition is often underdiagnosed due to its presentation.[310,311] Delirium-inducing medications (ie, steroids, anticholinergics) should be reduced or eliminated as much as possible.[312] Non-pharmacologic

interventions (eg, reorientation, cognitive stimulation, sleep hygiene) should be maximized before pharmacologic interventions are used. Caregivers should be supported in caring for their loved one and coping with this distressing condition.

Despite widespread use of antipsychotics for managing symptoms of delirium in palliative care, mixed evidence has been presented regarding use for delirium in patients with advanced cancer. In general, historical evidence supported the use of short-term, low-dose antipsychotics for managing symptoms of delirium with close monitoring for potential adverse effects.[313,314] Haloperidol is often used as a first-line agent, with alternative options such as olanzapine, risperidone, and quetiapine, titrating dose to optimal effect with the lowest possible dose.[315-317] However, conflicting data have also been published. In recent studies of patients in palliative care or critically ill patients in the ICU, antipsychotics such as haloperidol, risperidone, and ziprasidone were ineffective at significantly reducing symptoms of delirium.[318,319] Additionally, in one trial, the cohort receiving placebo with supportive care had longer overall survival times than the cohort receiving haloperidol.[318]

Benzodiazepines should not be used as initial treatment for delirium in patients not already taking them. However, benzodiazepines may be effective as an adjuvant to antipsychotics in the setting of persistent agitation, as demonstrated by a randomized controlled trial of lorazepam added to haloperidol for agitated delirium in patients with advanced cancer receiving palliative care.[320] 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-management medications should be titrated to optimal relief. Opioid dose reduction or rotation can also be considered for patients with severe delirium. RT can be considered for patients with delirium due to brain metastases; however, there are currently no data demonstrating improvement, and palliative efforts should be intensified with the awareness that delirium is a marker for “days not weeks” prognosis.[321-323]

For the dying patient, the focus should shift to family/caregiver support and education. Medications that are no longer necessary should be discontinued, and dose reductions of all other medications should be considered, especially if dependent on hepatic/renal function. Under- or overtreatment of pain can exacerbate delirium, as can fecal impaction or distended bladder; these should be excluded as potential causes. Opioid rotation can be considered (see NCCN Guidelines for Adult Cancer Pain) if the delirium is believed to be caused by neurotoxicity of the current opioid. If delirium is a result of disease progression, palliative care should be focused on symptom management and family support. Neuroleptic and benzodiazepine medications should have their dose increased and/or their route of administration changed to ensure adequate delirium symptom management.[324] 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 Guidelines for Distress Management for further discussion of delirium in patients with cancer.

Psychosocial Distress – Social Support/Resource Management

For distress related to psychological or psychiatric complications and spiritual or existential crisis, please see the NCCN Guidelines for Distress Management.

For best outcomes, psychosocial care should be integrated into routine cancer care across all disease stages and in both the inpatient and outpatient settings.[27,325-327] A recent systematic review of patients with advanced cancer identified psychosocial resources among the factors that promoted personal growth during the experience of cancer.[328]

For patients with estimated life expectancy ranging from years to months experiencing psychosocial distress, social support/resource management should be offered. Patient/family/caregiver(s)' coping and adjustment to the illness should be assessed, along with the safety of the environment and the availability of caregivers. In addition, it is important to ensure that the patient has adequate access to transportation and sufficient financial resources. Cultural issues, including the need for medical interpreters/translators unrelated to the patient, should be addressed. Support from social services (social worker, psychologist, and/or psychiatrist) may also be appropriate for the patient as well as caregivers and family members, and should be provided in the form of counseling, child life services, and art and music therapy (if available).[329-331] Personal, spiritual, or cultural issues related to the patient's illness and prognosis should be addressed.[332] Bereavement risk and risk for persistent complex bereavement disorder should be assessed.

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, family, and caregivers. Risk for persistent complex bereavement disorder 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.

Palliative Care Reassessment

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. The outcome measures for these guidelines are much more difficult to define than that for disease-specific NCCN Guidelines. The panel reviewed end-of-life care outcomes from several surveys of North American citizens.[333-336] 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 symptom management; 2) reduction of patient/family/caregiver distress; 3) acceptable sense of control; 4) decreased caregiver burden; 5) strengthened relationships; 6) optimized quality of life, personal growth, and enhanced meaning; and 7) advanced care planning in progress.

If the interventions are unacceptable upon reassessment, the oncology or palliative care team should reevaluate intervention options and intensify as possible. The oncology team should also consult specialized palliative care services, hospice, or an ethics committee. Consultation with a mental health professional and/or addiction specialist to evaluate and treat undiagnosed psychiatric disorders, substance abuse, and inadequate coping methods may also be necessary. If psychosocial distress persists, palliative care options should be intensified, and the patients should be managed according to the NCCN Guidelines for Distress Management.

Patients' treatment goals and expectations may change and evolve as disease progresses. Reassessment should be ongoing, with continuation or modification of life-expectancy-guided palliative care until the patient's death or survivorship.

End-of-Life Care Issues

Preparing Patients/Families/Caregivers for End-of-Life and Transition to Hospice Care

A multicenter survey of acute care hospitals revealed discordance between patients' stated values and corresponding treatment preferences for end-of-life care. The study highlighted the need for medical decision support to ensure that patient preferences were grounded in a clear

understanding of their illness and end-of-life treatment options.[337] Speciality palliative care consultation should 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.

For patients with an estimated life expectancy of years or years to months, health care professionals should engage in clear, consistent discussion with the patient, family, and caregiver(s) about prognosis and anticipated care needs on an ongoing basis. Advance care planning should be initiated, along with an assessment of decision-making capacity and the need to identify a surrogate decision maker. Providers should elicit values and preferences with respect to quality of life and determine need for specialized palliative care or eligibility and readiness for hospice care. When the patient's functional status indicates a 6- to 12-month prognosis, a dedicated "hospice information" visit with the oncologist may ease transition to hospice care in the future by preparing the patient, family, and caregiver(s), and reassuring them that their oncologist can remain involved.

For patients with an estimated life expectancy of months to weeks or weeks to days, the oncology team should assess patient/family/caregiver understanding of the dying process and provide education as needed. Providers should address potential need for transitions in care while ensuring continued involvement of the primary care physician and primary oncology team. Referrals should be made to hospice care agencies, as well as for psychosocial assessment, legacy work, grief counseling, spiritual assessment, and funeral/memorial service planning, as necessary. The goals and needs of the patient and family regarding the dying process should be respected.

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, family, and caregiver 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.

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. Advance care planning should be encouraged early and readdressed along the care continuum if not already completed. The patient's decision-making capacity should also be assessed, and a surrogate decision-maker identified. Recent studies have shown that these discussions frequently happen too late in the trajectory of disease, often during acute hospital care and often with health professionals other than the primary oncologist.[338-340] Earlier end-of-life care discussions have been associated with less aggressive care and increased use of hospice,[341,342] while less aggressive care has been associated with an improved quality of life.[343] Studies suggest that most patients with cancer would prefer to die at home,[344,345] but lack of timely advance care planning can render this impossible.

A randomized controlled trial of a structured intervention to facilitate end-of-life discussions (consisting of an information pamphlet and provider discussion) led to earlier designation of do-not-resuscitate orders and decreased the likelihood of patients dying in the hospital.[346] In addition, a recent study showed that electronic prompts and email reminders to doctors could increase rates of documentation of code status in patients with advanced lung cancer.[347] A 2015 systematic review summarizes the evidence base from randomized trials of interventions designed to promote shared decision-making and advance care planning in patients with serious illness.[348]

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/caregiver/health care team; and formal documents including advance directives, living wills, powers of attorney, health care proxy, or any other documents delineating specific limitations regarding life-sustaining treatments (eg, cardiopulmonary resuscitation, mechanical ventilation, and artificial nutrition/hydration). It may be helpful to determine the patient and family's prior experience(s) with end-of-life care. 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.[349]

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.

The patient's preferred location for receiving end-of-life care should be determined. Most patients with cancer would prefer to spend one's remaining time at home,[344,345] but sometimes their care needs are too great to be feasible in the home. Some patients request to receive end-of-life care in a skilled nursing facility or an in-patient hospice facility.[345,350] A prospective study showed that patients dying in an ICU had higher levels of physical and emotional distress compared with patients dying at home or in hospice. Additionally, caregivers of these patients had a greater incidence of prolonged grief disorder.[351] Providing palliative care services has been shown to decrease deaths in ICUs.[350] A recent retrospective cohort study showed that patients who wanted to be at home at the end of life were more likely to do so if they had daily hospice visits, if they were married, if they had advance directives, if they did not have moderate or severe pain, or if they had good performance status.[345] A second retrospective study suggested that referral to specialist palliative care at a greater interval of time prior to death increased the likelihood of patients dying at home or in hospice rather than in the hospital.[352] 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 should be clarified and confirmed. Providers should facilitate continued involvement of the primary care physician and primary oncology team. The desire for organ donation and/or autopsy should also be explored with the patient. The oncology team should ensure that the care provided is in compliance with the patient's advance care plan.

Requests for Hastened Death

The most appropriate initial response to a request for hastened death (ie, medical aid in dying, physician-assisted dying) is to explore the meanings behind that request and intensify palliative care interventions. The AAHPM has released a position statement and advisory brief regarding this topic with guidance for health care professionals on how to evaluate and respond to these requests.[353,354] The panel recommends that patients requesting hastened death should be referred to a palliative care specialist. Open exploration of the patient's request for hastened death may identify unmet needs and new palliative care interventions that may be helpful.[355] Concerns related to the withdrawal of life-sustaining treatment, voluntary cessation of eating and drinking, and/or sedation should be discussed with patients and families. Psychiatric consultation to evaluate and treat reversible causes of psychological suffering should be

considered. Patients should be assured that their health care team is committed to providing continuing care. Although medical aid in dying, under specified conditions, is legal in the states of California, Colorado, Hawaii, Montana, Oregon, Vermont, and Washington, euthanasia is not legal in any of the United States.[356-360] It is important for physicians to know the local legal status of medical aid in dying, as other states have pending legislation regarding either prohibiting or permitting medical aid in dying. Several organizations have released position statements and/or helpful websites on the issue of medical aid in dying (see Table 1).

Care of the Imminently Dying Hospitalized Patient

An imminently dying patient is defined as one within hours of death who is not stable enough for transport.[361] Caring for an imminently dying patient is intense for the patient, family, caregiver(s), and health care team. A recent international qualitative study described many of the common non-pharmacologic palliative care activities provided in the last days of life.[362] 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. If not already done, obtaining a hospice evaluation may also be helpful.

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. Approaches may include intensifying comfort care, discontinuation of unnecessary diagnostic tests and interventions, deactivation of implanted devices as indicated, alternate routes of medication administration if the oral route is not feasible, and managing terminal secretions, delirium, and dyspnea. Palliative sedation can be considered for refractory restlessness and agitation.[176,363,364] It is also important to be prepared 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. Open communication should occur between the patient, family, caregiver(s), and care team regarding the physical and psychological aspects of the dying process and the importance of honoring any advance directives. The care plan may also include consultation with social workers or chaplains to meet social and spiritual needs; counseling to promote healthy grieving; support for children/grandchildren; and education for parents on age-appropriate grieving processes.

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; securing a private room for the patient; and enabling family presence around-the-clock. If not already done, patient/family/caregiver wishes for resuscitation should be discussed and documented. If CPR is unlikely to be effective, providers should recommend other options for resuscitation such as "Do Not Resuscitate" (DNR), "Do Not Attempt Resuscitation" (DNAR), and "Allowing Natural Death" (AND) orders and promote comfort care. Providers should be aware that policies regarding resuscitation may differ based on treatment setting. A patient with a documented inpatient DNAR order may also require DNAR orders for out-of-hospital settings (eg, residential care, ambulance transport). In states where the MOLST/POLST has been established, it is important to complete this document, as it will protect the patient's wishes across all treatment settings.

Palliative Sedation

Palliative sedation may be considered for imminently dying patients (life expectancy of hours to days) with refractory symptoms that persist despite comprehensive, interprofessional palliative care. Palliative sedation to unconsciousness, in which the intended effect is deep sedation, remains

controversial.[365,366] If palliative sedation is being considered, a prognosis of imminent death should be confirmed. Informed consent must be obtained from the patient and/or a surrogate or family member following discussions of the patient's disease status, treatment goals, prognosis, and expected outcomes. Consent for palliative sedation must be accompanied by consent for discontinuation of life-prolonging therapies (such as artificial hydration/nutrition) and withholding of cardiopulmonary resuscitation, as these therapies would only serve to increase suffering in this case.

Palliative sedation has its ethical justification in the Doctrine of Double Effect,[367-372] which provides guidance in situations where an attempt to do good also produces harm (eg, providing medication for the relief of suffering that also causes respiratory depression). Several studies have investigated whether palliative sedation shortens survival. Results obtained from systematic reviews did not reveal a clear impact of palliative sedation on survival time, although many of the included studies lacked high-quality data.[373,374] A large prospective study in 2426 patients with advanced cancer provided additional evidence that continuous deep sedation provided by palliative care specialists did not significantly shorten survival time.[375] Prior to initiating palliative sedation, an ethics consult should be considered in accordance with institutional guidelines and state/national regulations.[366]

Palliative sedation is best performed by palliative care experts.[376] The most common sedatives used for palliative sedation are midazolam and propofol by parenteral infusions.[370] Recent studies suggested that palliative sedation may also be feasible in the home setting and could be utilized in patients who wish to die at home.[377,378]

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.[379-382] 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.[382] End-of-life care should be flexible enough to ensure that the death is viewed as a peaceful death by those involved.[382] 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."[383]

Final results of the prospective, longitudinal cohort Coping With Cancer study of 396 patients with advanced cancer and their caregivers were recently reported. The study found a higher quality of life in the last weeks of life in patients who avoided visits to the ICU and feeding tubes, did not die in the hospital, worried less, prayed or meditated, were visited by a pastor in the hospital or clinic, and felt a strong therapeutic alliance with their physicians.[343]

After-Death Care Interventions

Comprehensive palliative care for the patient's family and caregivers continues after the patient's death. Immediate issues include informing the family (if not present), offering condolences, and providing family time with the body. Chaplain involvement to assess family's desire for religious ritual or spiritual support may be helpful. Additional concerns 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); addressing concerns about organ donation or autopsy; facilitating funeral arrangements through completion of necessary

paperwork; and informing insurance companies and other health care professionals 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 grief should be identified and offered support and treatment.[384-386] Children of patients with cancer represent a uniquely at-risk population for psychosocial dysfunction. Additionally, a recent study suggested that certain predictors of prolonged grief could be identified in family caregivers at the time of the patient's entry to palliative care; these factors include severity of pre-death symptoms; condition of the caregiver's relationship to the patient; impact of caregiving duties on the caregiver's schedule; quality of family functioning; and level of optimism, especially if low.[387]

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. If not already recommended, providers should direct family members towards genetic screening, especially if the deceased patient was positive for known genetic markers that confer risk. For more information, see the NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast and Ovarian and Genetic/Familial High-Risk Assessment: Colorectal.

Putting Palliative Care Guidelines into Practice

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. Many approaches to this have been described, but there is no single best practice.[18-26,388]

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 interprofessional palliative care teams, including board-certified palliative care physicians and advanced practice providers, 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 begin with the diagnosis, and many palliative care questions should be considered early in the comprehensive cancer care plan. As the cancer progresses and the value of further anticancer therapy diminishes, palliative measures should be intensified. Clear and consistent discussion of goals, values, preferences, prognostic information, and therapeutic options can help patients, families, and providers make appropriate decisions in a shared manner.

Undergoing anticancer therapy should not preclude addressing end-of-life issues. Collaborating with palliative care experts on such matters 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 work to alleviate those fears by assuring patients that the members of the oncology and palliative care teams will work with them and their families regardless of what happens. Additionally, oncologists must discuss

prognosis with both the family and the palliative care team in order to anticipate and manage concerns commonly associated with the diagnosis and treatment of cancer.

As the disease progresses, many patients and families need help coping with the implications of increasing disease burden. Some patients and families have great difficulty accepting a poor prognosis and, as a result, do not engage in advance care planning.[389,390] This may be a sign of imperfect understanding of the disease and should be addressed directly and compassionately.[390] Palliative care supports ongoing education to help patients and families better understand and prepare for disease progression.

Oncologists should encourage advance care planning early in the disease trajectory in order to create a care plan that is consistent with the patients' wishes. In addition, advance care planning can lessen the burden of making 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.

Psychosocial Support for Oncology and Palliative Care Providers

After the loss of a patient, psychosocial support should be available for providers who have been involved in the patient's care. A bereavement or memorial ritual, such as a brief reading or moment of quiet, can be considered. Funeral attendance by health care professionals may also be considered. Health care professionals should 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.

Oncology and palliative care teams commonly encounter patient loss and deal with grief, and over time the resultant emotional distress can lead to compromised resilience, including provider burnout, compassion fatigue, and/or moral distress.[391-394] These syndromes can manifest as symptoms of depression, anxiety, fatigue, and low mental quality of life.[395] Personnel experiencing such symptoms should be identified and assisted. Considerable research has been dedicated to evaluating patterns of patient, family, and caregiver grief, and interventions to mediate this distress. Far less attention has been devoted to similar issues among health care providers and teams; further research is needed. For a summary of the literature on compassion fatigue and burnout among oncology providers, see reviews by Najjar and colleagues,[391] Shanafelt and Dyrbye,[395] and Sherman and colleagues.[396]

Although limited in quantity, most studies on compassion fatigue are derived from the oncology nursing literature. A large survey of hospice and palliative care providers (ie, clinical, administrative, allied health workers) revealed a strong correlation between burnout and compassion fatigue, and revealed the need for enhanced support of individuals in this field.[397] Additionally, a cross-sectional survey of nurses, medical assistants, and radiology technicians at a comprehensive cancer center revealed concerning levels of burnout and compassion fatigue in both inpatient and outpatient care settings.[398] A resiliency program was piloted and eventually scaled hospital-wide to educate providers on these issues and provide interventional strategies. Improvements in burnout and secondary traumatic stress were observed.[398,399] Several studies from the Mayo Clinic demonstrated that mindfulness training through the Stress Management and Resiliency Training (SMART) program was able to improve anxiety, stress, quality of life, and mindfulness among providers.[400-402] A recent meta-analysis of efficacy data on meditative interventions for health professionals demonstrated a small to moderate benefit according to measures of emotional exhaustion (effect size 0.37, 95% CI, 0.04–0.70), sense of personal accomplishment (effect size 1.18, 95% CI, 0.10–2.25), and life satisfaction (effect size 0.48, 95% CI, 0.15–0.81).[403]

Qualitative research on compassion fatigue interventions reveals that oncology clinicians rated the following resources as helpful: educational interventions, support programs or resources in the workplace, retreats, and self-care measures.[391,404] Unfortunately, despite the reported desire for such interventions, access can be limited. In a nationwide survey of oncology nurses, only 60% of survey respondents reported access to an employee assistance program, 45% reported no offerings of education addressing workplace coping, and 82% of respondents reported no off-site programs such as retreats.[404]

Generally, evidence-based interventions for compassion fatigue, moral distress, and burnout in physicians are lacking. When asked to provide useful preventative measures and coping strategies, palliative care specialists recommended emphasizing the rewarding aspects of their work and strategies for "enhanced meaning-making."[405] Experts in the field have also highlighted the importance of self-awareness and self-care measures for oncologists and palliative care specialists to decrease levels of compassion fatigue.[406] To this end, self-care was established as a core competency area for fellows in hospice and palliative medicine.[406] Examples and evidence for additional preventative strategies and solutions for oncologist burnout have been reviewed by Shanafelt and Dyrbye.[395]

Conclusion

These guidelines are intended to help oncology teams incorporate palliative care into their practice and thereby provide the best and most comprehensive cancer treatment possible for patients with incurable cancer. Patients with advanced disease may be overly optimistic about their chances of cure and survival, and this can have a negative effect on their quality of life. One study found that those who overestimated their survival were more likely to die a bad death.[93] Using a decision aid, Smith et al found that most patients want honest information, even if it is bad news.[407] Although use of the decision aid typically took 20 minutes and was challenging for oncologists, it did not cause patients to give up hope or become distressed. Physician-led discussion of disease progression and death can improve quality of care and quality of life for both patients and families.[408] Providing information in a collaborative manner protects the autonomy of patients to make informed decisions based on potential treatment outcomes.[409] Palliative care can help patients and families set realistic expectations and meet short- and longer-term goals, such as important life-cycle events. Much of the care outlined in these guidelines is geared toward a different hope than that for cure of the disease itself.[101,407,410] Even when cure is no longer possible, hope remains: hope for dignity, comfort, and closure and for growth at the end of life. It is our hope that these guidelines will help oncology and palliative care professionals together create a better future for patients, families, and providers.

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.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

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

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

www.hpna.org/
Hospice & 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

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

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

www.cancerpatienteducation.org
Cancer Patient Education Network (CPEN): Healthcare professional organization for sharing experiences and best practices in all aspects of cancer patient 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/palliative-care-leadership-centers/
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

Physician-Assisted Dying

Statement on Physician-Assisted Dying approved by the AAHPM Board of Directors on June 24, 2016: http://aahpm.org/positions/pad

[a] All websites accessed Jan 2019.

Adapted with permission from Meier DE. Improving Palliative and Supportive Care in Cancer Patients. Oncology 2005;19(10).

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