



National Comprehensive  
Cancer Network®

**NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)**

# **Palliative Care**

Version 1.2024 — February 16, 2024

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▩ Geriatric medicine	£ Supportive care including hospice and palliative care medicine, pain management
‡ Hematology/Hematology oncology	Σ Oncology Pharmacy
‡ Internal medicine	Ψ Neurology/Neuro-oncology
† Medical oncology	* Discussion Section Writing Committee
€ Pediatric oncology	
θ Psychiatry, psychology, including health behavior	
§ Radiation oncology	



### [NCCN Palliative Care Panel Members](#) [Summary of the Guidelines Updates](#)

[Definition and Standards of Palliative Care \(PAL-1\)](#)

[Palliative Care General Overview \(PAL-2\)](#)

[Indications and Assessment by Oncology Team \(PAL-3\)](#)

[Oncology Team Interventions and Reassessment \(PAL-6\)](#)

[Consideration for Consultation with Specialty Palliative Care \(PAL-7\)](#)

[Shared Decision-Making Considerations \(PAL-9\)](#)

[Symptoms: Pain \(PAL-10\)](#)

[Symptoms: Dyspnea \(PAL-11\)](#)

[Symptoms: Anorexia/Cachexia \(PAL-13\)](#)

[Symptoms: Nausea and Vomiting \(PAL-15\)](#)

[Symptoms: Constipation \(PAL-17\)](#)

[Symptoms: Diarrhea \(PAL-18\)](#)

[Symptoms: Malignant Bowel Obstruction \(PAL-20\)](#)

[Symptoms: Sleep/Wake Disturbances Including Insomnia and Sedation \(PAL-22\)](#)

[Symptoms: Delirium \(PAL-23\)](#)

[Malignant Wounds \(PAL-25\)](#)

[Social Support/Resource Management \(PAL-26\)](#)

[Preparing Patients/Families/Caregivers for End of Life and Transition to Hospice Care \(PAL-28\)](#)

[Advance Care Planning \(PAL-29\)](#)

[Response to Requests for Hastened Death \(PAL-31\)](#)

[Shared Decision-Making in the Care of the Imminently Dying Hospitalized Patient \(PAL-32\)](#)

[Proportional Sedation \(PAL-33\)](#)

[After-Death Interventions \(PAL-34\)](#)

[Palliative Care Drug Appendix \(PAL-A\)](#)

[Abbreviations \(ABBR-1\)](#)

[Please see NCCN Guidelines for Distress Management](#)

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

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See [NCCN Categories of Evidence and Consensus](#).

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

Updates in Version 1.2024 of the NCCN Guidelines for Palliative Care from Version 2.2023 include:

#### Global Changes

- "Anticancer" modified to "cancer"
- "If unacceptable" modified to "if ongoing needs"
- "Acceptable outcomes" modified to "outcomes"
- "Psychosocial" modified to "psychosocial-spiritual"
- "Palliative care specialist" modified to "specialty palliative care"

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

#### PAL-2

##### • Indications

- ▶ **Bullet 9 modified:** ~~Advanced Cancers~~ associated with high morbidity ~~and~~ or mortality
- ▶ **Bullet 11 modified:** Evidence of worsening prognosis, ~~including:~~ (PAL-3)
- ▶ **Bullet removed:** Spiritual/existential distress
- ▶ **Bullet added:** Complexities related to social determinants of health
- ▶ **Sub-bullets removed:**
  - ◇ Poor performance status (eg, ECOG  $\geq 3$  or KPS  $\leq 50$ )
  - ◇ Cachexia
  - ◇ Persistent hypercalcemia
  - ◇ Brain or cerebrospinal fluid metastasis
  - ◇ Persistent delirium
  - ◇ Malignant bowel obstruction
  - ◇ Superior vena cava (SVC) syndrome
  - ◇ Spinal cord compression
  - ◇ Malignant effusions
  - ◇ Need for palliative stenting or venting gastrostomy
- **Assessment, present/ongoing reassessment, bullet 11 modified:** *Criteria Consideration* for consultation with ~~palliative care specialist~~ *specialty palliative care*



Updates in Version 1.2024 of the NCCN Guidelines for Palliative Care from Version 2.2023 include:

• **Interventions**

- ▶ **Bullet 13 modified: Response to requests for hastened death (~~physician-assisted dying~~ *medical aid in dying [MAID]*)**
- ▶ **Bullet 15 modified: ~~palliative~~ *proportional* sedation**

**PAL-3**

• **Indications**

- ▶ **Bullet removed: Spiritual/existential distress**
- ▶ **Bullet 7 added: Complexities related to social determinants of health**
- ▶ **Bullet 9 modified: ~~Advanced~~ Cancers associated with high morbidity ~~and~~ *or* mortality**
- ▶ **Sub-bullets removed:**
  - ◊ **Persistent hypercalcemia**
  - ◊ **Brain or cerebrospinal fluid metastasis**
  - ◊ **SVC syndrome**
  - ◊ **Spinal cord compression**
  - ◊ **Malignant effusions**
  - ◊ **Need for palliative stenting or venting gastrostomy**
- ▶ **Sub-bullet 4 modified: Malignant bowel obstruction *requiring venting gastrostomy***

- **Assessment, bullet 7 modified: ~~Criteria~~ *Consideration* for consultation with a ~~palliative care specialist~~ *specialty palliative care*. (Also for PAL-5)**

**PAL-6**

• **Oncology Team Interventions**

- ▶ **Bullet 3 added: Evaluate and treat undiagnosed mental health problems**
- ▶ **Bullet 4, sub-bullets removed:**
  - ◊ **Mental health and social services**
  - ◊ **Spiritual care**
  - ◊ **Health care interpreters**
  - ◊ **Others**
- ▶ **Bullet 4, sub-bullets added:**
  - ◊ **Mental health**
  - ◊ **Psychosocial-spiritual services**
  - ◊ **Behavioral health**
  - ◊ **Addiction specialist**
  - ◊ **Other specialists**

- **Reassessment, outcomes, bullet removed: Patient satisfied with response to anticancer therapy**

• **Reassessment, if ongoing needs**

- ▶ **Bullet added: Assess for communication barriers and address as needed (eg, translation services, improved literacy of materials, palliative care consult)**
- ▶ **Bullet removed: Evaluate and treat undiagnosed psychiatric disorders, and substance use disorders**
- ▶ **Sub-bullet removed: Consult with the following**
- ▶ **Sub-sub-bullets removed:**



Updates in Version 1.2024 of the NCCN Guidelines for Palliative Care from Version 2.2023 include:

- ◇ Mental health professional
- ◇ Addiction specialist

#### [PAL-7](#)

- Page title modified: ~~Criteria Consideration~~ for Consultation with Palliative care Specialist *Specialty Palliative Care* (Also for PAL-8)
- Assessment, bullet 2, sub-bullet 2 modified: ~~Advanced disease process~~ *Disease refractory to cancer treatment*
- Assessment, bullet 2, sub-bullet 4 modified: ~~Rapidly Progressive~~ functional decline or persistently poor performance status
- Assessment, bullet 12 modified: Communication ~~barriers~~ *needs*
- Assessment, bullet 12 sub-bullet removed: Physical barriers
- Assessment, bullet added: Patient/family requests

#### [PAL-8](#)

- Bullet removed: Family/caregiver challenges
- Bullet removed: Intensely dependent relationship(s)
- Bullet 1 modified: High risk for persistent ~~complex bereavement disorder~~ complicated grief
- Bullet 3 modified: Substance use ~~disorder~~ *impacting care*
- Bullet 6 modified: ~~Family discord~~ *Family/caregiver discord impacting care*
- Bullet 7 modified: Spiritual or existential ~~crisis~~ *distress*
- Bullet 10 added: Other complexities related to social determinants of health

#### [PAL-9](#)

- Interventions, Years to months
  - ▶ Bullet 2 modified: Discuss whether ~~anticancer therapy is palliative or curative~~ *cancer therapy is curative or noncurative*
  - ▶ Bullet 3 added: Cultivate prognostic awareness
  - ▶ Bullet 7 modified: Assess for appropriateness of palliative radiation therapy (RT) or interventional procedures *that are aligned with goals of care*
  - ▶ Bullet removed: Consider palliative procedures that are in line with goals of care
  - ▶ Bullet 8 modified: Provide ~~primary palliative care, including anti-cancer treatment~~ and disease-related symptom management and encouragement of advance care planning
  - ▶ Bullet 11 added: Consider rehabilitation services and physical activity aligned with goals of care
- Interventions, Months to weeks
  - ▶ Bullet 4 modified: Assess for appropriateness of palliative RT therapies or interventional procedures (*eg, single fraction*)
  - ▶ Bullet 5 modified: Consider discontinuation of cancer treatment not ~~directly addressing a symptom~~ *complex aligned with goals of care*
  - ▶ Bullet 7 modified: Offer goal-directed supportive care, ~~including referral to specialized palliative care services or hospice~~
  - ▶ Bullet 8 modified: Offer education and support related to care at end of life *including referral to specialized palliative care services or hospice*
  - ▶ Bullet 10 added: Explore culturally/spiritually significant rituals/ceremonies important at end of life

#### [PAL-9A](#)

- Reassessment if ongoing needs
  - ▶ Bullet 1 modified: ~~Change or~~ *Consider discontinuation of anticancer therapy*

#### [PAL-10](#)



Updates in Version 1.2024 of the NCCN Guidelines for Palliative Care from Version 2.2023 include:

- Reassessment, outcomes, bullet 2 modified: ~~Reduction of Patient/family/caregiver distress~~ *mitigated*
- Reassessment, if ongoing needs, bullet 4 added: Optimize communication
- Footnote added: For patients with a life expectancy of multiple weeks, consider single-fraction palliative RT for painful bone metastases.

#### PAL-11

- Interventions, years to weeks
  - ▶ Bullet 3 added: Consider discontinuing therapies that may be causing dyspnea
  - ▶ Bullet 4 modified: Treat potentially reversible underlying causes/comorbid conditions *using*:
  - ▶ Bullet 4, sub-bullet 1 modified: Radiation/chemotherapy/*interventional strategies as appropriate*
  - ▶ Bullet 4, sub-bullet 2 added: If immunotherapy-induced, see NCCN Guidelines for Management of Immunotherapy-Related Toxicities
  - ▶ Bullet 5, sub-bullet removed: Consider benzodiazepines if coexisting anxiety

#### PAL-12

- Bullet 6, sub-bullet 2
  - ▶ Sub-sub-bullet 1 modified: Oxygen if ~~hypoxic~~ *hypoxia present* and/or subjective relief is reported
  - ▶ Sub-sub-bullet 3 modified: ~~Benzodiazepines~~ *Consider benzodiazepines when opioids and other non-pharmacologic measures have failed to control dyspnea*
  - ▶ Sub-bullet added: Noninvasive positive-pressure ventilation (eg, CPAP, BiPAP) support if clinically indicated for severe reversible condition
- Bullet 7 modified: Reduce excessive secretions with *non-pharmacologic interventions and* anti-secretory agents
- Bullet 7, sub-bullet 1 added: Reduce IV fluids and consider repositioning

#### PAL-14

- Interventions, Months to days
  - ▶ Bullet removed: Consider appetite stimulant
  - ▶ Bullet 4 added: Counsel patients and family about benefits, risks (eg, thrombosis), and options for pharmacologic management of cachexia
  - ▶ Bullet 6, sub-bullet 6 added: Consider nutritional consult
  - ▶ Bullet 6, sub-bullet 7 added: Eating for pleasure may be considered, but should not be forced upon patients with no hunger or thirst
- Reassessment, outcomes, bullets removed
  - ▶ Decreased caregiver burden
  - ▶ Strengthened relationships
  - ▶ Optimized quality of life
  - ▶ Personal growth and enhanced meaning

#### PAL-15

- Interventions
  - ▶ Bullet 1 added: Consider treatment with corticosteroids and a proton pump inhibitor, while definitive treatment is selected.
  - ▶ Bullet 3 modified: Screen for potentially reversible causes/*common etiologies*:
  - ▶ Bullet 3, sub-bullet 6 modified: ~~Gastric outlet~~ *Gastrointestinal (GI)* obstruction from intra-abdominal tumor or liver metastasis
  - ▶ Bullet 3, sub-sub-bullet 4 added: Consider interventional procedures
  - ▶ Bullet removed: NCCN Guidelines for Management of Immunotherapy-Related Toxicities
  - ▶ Bullet 9 added: If immunotherapy-induced, see NCCN Guidelines for Management of Immunotherapy-Related Toxicities
- Footnote added: Do not give metoclopramide in patients with complete gastric outlet obstruction.



Updates in Version 1.2024 of the NCCN Guidelines for Palliative Care from Version 2.2023 include:

#### [PAL-16](#)

- If ongoing needs, bullet 3 modified: Consider ~~palliative~~ *proportional* sedation

#### [PAL-17](#)

- Interventions

- ▶ Bullet 5 modified: Treat other causes (eg, hypercalcemia, hypokalemia, hypothyroidism, diabetes mellitus, medications, *side effects of immunotherapy*)
- ▶ Bullet removed: Consider adding other laxatives
- ▶ Bullet 11 modified: ~~Titrate laxative agents to achieve desired frequency~~ Consider peripherally acting mu-opioid receptor antagonist (PAMORA) *or secretory agents* for opioid-induced constipation
- ▶ Bullet 12 modified: ~~Administer tap water enema until clear~~ *Administer enema until clear: eg, tap water, soap suds, mineral oil, lactulose*
- ▶ Bullet removed: Consider use of a prokinetic agent

#### [PAL-18](#)

- Screening and Assessment, bullet 1 modified: Evaluate diarrhea severity and *potential* causes
- Grading modified: Determine Diarrhea Severity/Grade
  - ▶ *Mild/Grade 1*
  - ▶ *Moderate/Grade 2*
  - ▶ *Severe/Grade 3*
  - ▶ *Severe/Grade 4*
- Interventions
  - ▶ Sub-bullet added: If immunotherapy-induced, see NCCN Guidelines for Management of Immunotherapy-Related Toxicities
  - ▶ Bullet added: Consider endoscopy if diagnostic uncertainty
- Footnotes added:
  - ▶ Euvolemic and no electrolyte abnormalities
  - ▶ Hypovolemia plus/minus electrolyte abnormalities
  - ▶ Severe hypovolemia and/or electrolyte abnormalities

#### [PAL-19](#)

- Screening assessment and bullet removed: Provide immediate antidiarrheal therapy indicated by grade
- Grade added: Any grade
- Intervention, any grade
  - ▶ Bullet added: Treat underlying cause as appropriate
  - ▶ Bullet added: If immunotherapy-induced diarrhea, see NCCN Guidelines for Management of Immunotherapy-Related Toxicities
  - ▶ Bullet added: Provide IV fluids and hydration if patient is unable to tolerate oral fluids
- Mild/Grade 1
  - ▶ Bullet removed: If chemotherapy induced, decrease or delay the next dose of chemotherapy
  - ▶ Bullet removed: Provide oral hydration and electrolyte replacement
  - ▶ Bullet 1 modified: ~~Initiate~~ *Consider* antidiarrheal agents (eg, loperamide) ~~if infection ruled out~~
- Moderate/Grade 2
  - ▶ Bullet 2 modified: ~~Initiate/continue~~ antidiarrheal agents—~~as above if infection ruled out~~
  - ▶ Bullet removed: If chemotherapy-induced, decrease or delay the next dose of chemotherapy
  - ▶ Bullet removed: If immunotherapy-mediated diarrhea, consider

[Continued](#)





Updates in Version 1.2024 of the NCCN Guidelines for Palliative Care from Version 2.2023 include:

- ▶ Sub-bullet removed: Corticosteroids
- ▶ Sub-bullet removed: Infliximab
- ▶ Sub-bullet removed: Probiotics
- ▶ Sub-bullet removed: See Management of Immunotherapy-Related Toxicity Guidelines for immunotherapy-related diarrhea
- Severe/Grades 3/4
  - ▶ Bullet removed: For GVHD diarrhea, consider limiting diet, steroids, and IV nutrition

#### [PAL-20](#)

- Months to days, bullet 2 modified: Assess patient's goals for treatment to guide choice of intervention (eg, decrease NV, ~~allow patient support the desire to eat, decrease pain, allow support patient to go home/to hospice~~)

#### [PAL-21](#)

- Procedural interventions
  - ▶ Bullet 2 modified: Endoscopic management (*eg, G-tube for drainage, endoscopic stent placement*)
  - ▶ Sub-bullet removed: Percutaneous endoscopic G-tube for drainage
  - ▶ Sub-bullet removed: Endoscopic stent placement
  - ▶ Sub-bullet removed: G-tube for drainage

#### [PAL-23](#)

- Interventions for severe delirium (agitation)
  - ▶ Bullet 3 modified: Consider addition of ~~low-dose benzodiazepines with or without~~ antipsychotic medications if ~~symptoms~~ *severe agitation* persists
  - ▶ Bullet removed: If agitated delirium is refractory to high doses of neuroleptics, consider adding benzodiazepine
  - ▶ Bullet 6 added: Encourage supportive caregiver presence at bedside

#### [PAL-24](#)

- Interventions, weeks to days
  - ▶ Bullet 2 added: Maximize nonpharmacologic interventions (optimize sleep wake cycle; address sensory impairment; provide glasses, hearing aids)
  - ▶ Bullet removed: Provide appropriate upward dose titration of antipsychotic agents
  - ▶ Bullet 8 modified: Provide appropriate upward dose titration of benzodiazepines *with or without antipsychotics* for patients with refractory agitation ~~despite high doses of neuroleptics~~
  - ▶ Bullet 9 added: Encourage supportive caregiver presence at bedside
  - ▶ Bullet 10 added: Support caregivers
  - ▶ Bullet removed: Consider rectal or intravenous administration of antipsychotic with or without benzodiazepine

#### [PAL-25](#)

- Interventions, weeks to days
  - ▶ Sub-bullet 5 modified: Pain: treat according to *NCCN Guidelines for Adult Cancer Pain*; see *PAL-9 and PAL-10*; use non-absorbent dressing or reduce frequency if associated with dressing changes; topical opioid and/or local anesthetic; complementary therapies

#### [PAL-26](#)

- Interventions, years to weeks

[Continued](#)**UPDATES**



Updates in Version 1.2024 of the NCCN Guidelines for Palliative Care from Version 2.2023 include:

- ▶ **Bullet 2 added: Complexities related to social determinants of health**
- ▶ **Bullet 7 modified: ~~Assess risk for persistent complex bereavement disorder~~ *Periodically assess and monitor family/caregiver for risk factors associated with complicated grief***

#### **PAL-27**

- **Interventions, weeks to days, bullet 3 modified: ~~Explain~~ *Educate* about the dying process and expected events to the patient/caregiver(s)/family members**

#### **PAL-28**

- **Assessment/Interventions, years to months, bullet 4 modified: ~~Determine need~~ *Introduce, educate, and assess need* for specialized palliative care or eligibility and readiness for hospice care**
- **Assessment/Interventions, months to days, sub-bullet 2 modified: *Spiritual assessment screening***

#### **PAL-29**

- **Reassessment, if ongoing needs, bullet 5 modified: Consider referral to *chaplain/spiritual care counselor***

#### **PAL-31**

- **Heading modified: Response to Requests for Hastened Death ~~or Medical Aid in Dying (MAID)~~**
- **Bullet 1 modified: 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~~ *may* 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~~ *medical aid in dying (MAID)* is never morally acceptable. Clarifying these meanings may enlarge the range of useful therapeutic options and might reduce the patient's wish to die.**
- **Bullet 5 modified: ~~Request~~ *Consider* a consult with a mental health professional to evaluate and treat reversible causes of psychological suffering.**
- **Bullet 9 modified: Know the local legal status *and local health system policies and procedures* of MAID. Some patients and clinicians may be confused about legal/ethical distinctions; treatment withdrawal and aggressive treatments for symptoms, such as pain, are not requests for hastened death. ~~MAID is currently legal in 10 U.S. jurisdictions; euthanasia is not legal anywhere in the United States.~~**

#### **PAL-32**

- **Physical**
  - ▶ **Sub-bullet 9 modified: Treat ~~unclearable~~ terminal secretions (death rattle)**
  - ▶ **Sub-sub bullet added: Educate patient and caregiver**
  - ▶ **Sub-sub bullet modified: ~~Avoid deep suctioning~~ *Provide gentle oropharyngeal suctioning (avoid deep suctioning)***
  - ▶ **Sub-sub bullet added: Utilize non-pharmacologic interventions first before antisecretory agents**
  - ▶ **Sub-bullet 12 modified: Consider ~~palliative proportional sedation~~ for refractory ~~restlessness and agitation symptoms~~**
- **Psychosocial-spiritual**
  - ▶ **Sub-bullet 1 modified: Educate the patient/family/caregiver about *the signs and symptoms of dying and* the rationale for discontinuation of treatments or medications that may not add to the patient's comfort**

#### **PAL-33**

- **Title updated: *Palliative Proportional Sedation***
- **Bullet 1 modified: *Palliative Proportional sedation (formerly known as palliative sedation)* is the intentional lowering of awareness towards, and including, unconsciousness for patients with severe and refractory symptoms *with primary goal of symptom relief including alleviation of suffering.***



Updates in Version 1.2024 of the NCCN Guidelines for Palliative Care from Version 2.2023 include:

- **Bullet 4 modified:** "A patient who is suffering from a terminal illness and who is experiencing great pain has no legal barriers to obtaining medication, from qualified physicians, to alleviate suffering, even to the point of unconsciousness and hastening death." -Justice O'Connor (see *Vacco v Quill* and *Washington v Glucksberg*, 1997). ~~Palliative sedation is, however, controversial for existential suffering, and many providers do not ethically support the practice for patients not likely to die within 2 weeks, because at that point the absence of hydration and food can become the immediate physiologic cause of death. However, for acutely dying patients the current body of literature supports that palliative sedation does not hasten death.~~

#### [PAL-34](#)

- **Assessment, bullet 3 modified:** Consistent with clinical, cultural, *spiritual*, and ethical standards

#### [PAL-A 1 of 5](#)

- **Dyspnea**
  - ▶ Life expectancy modified: Years; Year to Months; and Months to Weeks; ~~Weeks to Days (dying patient)~~
  - ▶ Sub-bullets removed:
    - ◊ Opioid tolerance should be taken into consideration with dosing
    - ◊ Consider alternatives to morphine in patients with known renal compromise
  - ▶ Sub-bullet added: Base dosing on patient's opioid requirement. If patient's opioid requirement is unknown, start with low doses and titrate up as appropriate.
  - ▶ Bullet removed: Anxiety: Lorazepam, 0.25–1 mg PO q1h PRN if benzodiazepine naïve
- **Row added:** Dyspnea, weeks to days
- **Secretions bullet modified:** Excessive secretions: Glycopyrrolate, 0.2–0.4 mg IV or SC every 4 h PRN (*less sedating*), scopolamine, PRN/1.5 mg patches, 1–~~3~~ 2 patches every 72 h OR atropine, 1% ophthalmic solution 1–2 drops SL every 2 h PRN (*caution in asthma*), OR hyoscyamine, 0.125–0.25 mg PO or SL every 4 h with max dose of 1.5 mg daily
- **Anorexia/Cachexia**
  - ▶ Bullet 3 modified: Low/no appetite: Megestrol acetate, ~~480–600 mg/d~~ PO2 OR olanzapine, 2.5–5 mg/d PO OR corticosteroid-PRN-*dexamethasone 3–8 mg/d OR cannabinoid-PRN*
  - ▶ Bullet 4 added: Clinicians may choose not to prescribe pharmacologic intervention for cancer cachexia treatment

#### [PAL-A 2 of 5](#)

- **Nausea and vomiting**
  - ▶ Line added: Common Etiologies
  - ▶ Bullet 2 modified: Gastroparesis: Metoclopramide, 5–10 mg PO QID 30 min before meals and QHS (*avoid in setting of complete bowel obstruction*)
  - ▶ Bullet 5 modified: 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~~
  - ▶ Bullet 7 added: Olanzapine, 2.5–5 mg PO 1–2 times daily starting QHS
- **Constipation**
  - ▶ Bullet 1 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~~ *Start with an osmotic laxative if patient can tolerate the volume of liquid (polyethylene glycol BID) and add stimulant laxatives (senna BID or bisacodyl daily–TID) to achieve a goal of one non-forced bowel movement every 1–2 days*
  - ▶ Bullet removed: General: Add bisacodyl, titrate to 10–15 mg PO daily–TID with a goal of one non-forced bowel movement every 1–2 days

**Updates in Version 1.2024 of the NCCN Guidelines for Palliative Care from Version 2.2023 include:**

- ▶ **Bullet 3 modified: Resistant opioid-induced constipation: ~~Consider methylnaltrexone, 8 or 12 mg/dose SC QOD; linaclotide, 72–145 mcg/d PO; naloxegol, 12.5–25 mg/d PO~~**
- ▶ **Sub-bullet added: If oral therapy is not effective, try enema**
- ▶ **Sub-bullet added: Consider methylnaltrexone, 8 or 12 mg/dose SC QOD; naloxegol 12.5–25 mg daily PO; naldemedine 0.2 mg daily PO; lubiprostone 24 mcg BID PO; linaclotide 145–290 mcg daily PO**

**PAL-A 3 of 5**

- **Diarrhea (years to weeks)**
  - ▶ **Grades modified:**
    - ◊ **Grade 1 (*mild*)**
    - ◊ **Grade 2 (*moderate*)**
    - ◊ **Grades 3/4 (*severe*)**
  - ▶ **Grade 1, bullet 3 modified: ~~If not on opioids:~~ Diphenoxylate/atropine 1–2 tabs PO every 6 h PRN, maximum 8 tabs/d (Also for grades 2 and 3/4)**
  - ▶ **Grade 2, bullet 4 modified: C. diff-induced: Metronidazole, 500 mg PO/IV ~~QID~~ TID x 10–14 days; vancomycin, 125–500 mg PO QID x 10–14 days**
  - ▶ **Grade 2, bullet removed: Immunotherapy-related: Dexamethasone, 4–8 mg/d; infliximab, 5 mg/kg every 2–6 weeks**
- **Diarrhea (weeks to days)**
  - ▶ **Bullet 2 modified: ~~Initiate or increase dose of around-the-clock opioid~~ Consider *tincture of opium***
  - ▶ **Bullet 5 modified: Consider glycopyrrolate, 0.2–0.4 mg IV/SC every 4 h PRN**

**PAL-A 4 of 5**

- **Page extensively modified**

**PAL-A 5 of 5**

- **Delirium, years to weeks**
  - ▶ **Bullet 1 modified: Use *Maximize* nonpharmacologic approaches when possible**
- **Delirium, weeks to days**
  - ▶ **Bullet 4 modified: Consider chlorpromazine, 25–~~100~~50 mg PO/PR QHS with or without lorazepam, 0.5–2 mg SC/IV every 6 h**
- **Palliative *Proportional* Sedation**
  - ▶ **Bullet 1 added: Refer to institutional guidelines and policy**

**Definition of Palliative Care<sup>a,b</sup>**

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

**Standards of Palliative Care<sup>c,d</sup>**

- **Palliative care should be provided by the primary oncology team and augmented as needed by collaboration with an interprofessional team of palliative care experts.**
- **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 patients with cancer should be screened for palliative care needs at their initial visit, at appropriate intervals, and as clinically indicated (see [PAL-2](#) and [PAL-3](#)).**
- **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.**
- **Interprofessional palliative care teams, including but not limited to board-certified palliative care physicians, advanced practice providers, nurses, social workers, chaplains, and pharmacists, should be readily available to provide consultative or direct care to patients/families/caregivers and/or health care professionals who request or require their expertise.**
- **Quality of palliative care should be monitored by institutional quality improvement programs.**

<sup>a</sup> Hui D, et al. J Pain Symptom Manage 2012;43:582-592.

<sup>b</sup> Seaman JB, et al. J Palliat Med 2020;23:1157-1158.

<sup>c</sup> Ferris FD, et al. J Clin Oncol 2009;27:3052-3058.

<sup>d</sup> 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. Available at: [www.nap.edu/read/18748/chapter/1](http://www.nap.edu/read/18748/chapter/1).

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# NCCN Guidelines Version 1.2024 Palliative Care

## INDICATIONS<sup>e,f</sup>

- Uncontrolled symptoms
- Moderate-to-severe distress related to cancer diagnosis and/or cancer therapy
- Serious comorbid physical and/or psychiatric conditions
- Complex psychosocial-spiritual needs
- Patient/family/caregiver concerns about course of disease and decision-making
- Patient/family/caregiver requests for palliative care
- Complexities related to social determinants of health
- Patient request for hastened death
- Cancers associated with high morbidity or mortality
- Poor prognostic awareness
- Evidence of worsening prognosis ([PAL-3](#))

## ASSESSMENT

- Ongoing reassessment
- Benefits/burdens of cancer therapy
  - Financial toxicity
  - Decision-making capacity
  - Coping strategies
  - Personal goals/values/expectations
  - Symptoms
  - Functional status
  - Psychosocial or spiritual distress
  - Educational and informational needs
  - Cultural factors affecting care
  - Consideration for consultation with specialty palliative care ([PAL-7](#))

## INTERVENTIONS<sup>f</sup>

- Cancer therapy
- Appropriate treatment of comorbid physical and psychosocial-spiritual conditions
- Coordination of care with other health care providers
- Promote adaptive coping
- Symptom management
- Advance care planning
- Psychosocial-spiritual support
- Culturally congruent care
- Resource management/social support
- Consultation with speciality palliative care
- Transition to end-of-life care including hospice referral as appropriate
- Response to request to withdraw or withhold life-sustaining treatment
- Response to requests for hastened death (medical aid in dying [MAID])
- Care of imminently dying hospitalized patient
- Proportional sedation
- Normalization of anticipatory grief and bereavement education and support

## REASSESSMENT

- Outcomes:
- Patient satisfied with response to cancer therapy
  - Adequate symptom management
  - Reduction of patient/family/caregiver distress
  - Acceptable sense of control
  - Decision-making capacity
  - Decreased caregiver stress and burden
  - Strengthened relationships
  - Optimized quality of life
  - Personal growth and enhanced meaning

If ongoing needs

- Re-evaluate intervention options and intensify as possible
- Consult with other clinicians and refer to specialist if available

## AFTER-DEATH INTERVENTIONS

- For family and caregiver(s):
- Immediate after-death care
  - Psychological bereavement support
  - Cancer risk assessment and modification
- For health care team:
- General support (ie, debriefing)

[Footnotes on PAL-2A](#)

[Assessment by Oncology Team \(PAL-3\)](#)

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### FOOTNOTES

<sup>e</sup> Patients with one or more positive indicators may benefit from a care plan developed by an interprofessional team of physicians, nurses, social workers, mental health professionals, chaplains, advanced practice clinicians, and other health care professionals.

<sup>f</sup> Oncologists should integrate palliative care into general oncology care. Early consultation/collaboration with a specialty palliative care/hospice team should be considered to improve quality of life and survival.

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- Patient/family/caregiver requests for palliative care
- Complexities related to social determinants of health
- Patient request for hastened death
- Cancers associated with high morbidity or mortality
- Poor prognostic awareness
- Evidence of worsening prognosis, including but not limited to:
  - ▶ Poor performance status (eg, ECOG ≥3 or KPS ≤50)
  - ▶ Cachexia
  - ▶ Persistent delirium
  - ▶ Malignant bowel obstruction requiring venting gastrostomy

### ASSESSMENT BY ONCOLOGY TEAM

- Benefits/burdens of cancer therapy<sup>g,h</sup> → [PAL-4](#) and [PAL-5](#)
- Symptoms
- Psychosocial-spiritual distress
- Personal values/goals/expectations → [PAL-4](#) and [PAL-5](#)
- Educational and informational needs
- Cultural factors affecting care
- Consideration for consultation with specialty palliative care → [PAL-7](#)

Present →

Not present ↓

- Inform the patient/family/caregiver about palliative care services
  - ▶ Anticipate symptoms and discuss preventive measures
  - ▶ Discuss advance care planning
  - ▶ Rescreen at next visit

<sup>e</sup> Patients with one or more positive indicators may benefit from a care plan developed by an interprofessional team of physicians, nurses, social workers, mental health professionals, chaplains, advanced practice clinicians, and other health care professionals.

<sup>f</sup> Oncologists should integrate palliative care into general oncology care. Early consultation/collaboration with a specialty palliative care/hospice team should be considered to improve quality of life and survival.

<sup>g</sup> See FEV-D in the [NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections](#) for an approach to assess for the risk of serious complications in patients with neutropenic fever.

<sup>h</sup> For an approach to decision-making in older adults and geriatric screening tools, see the [NCCN Guidelines for Older Adult Oncology](#).

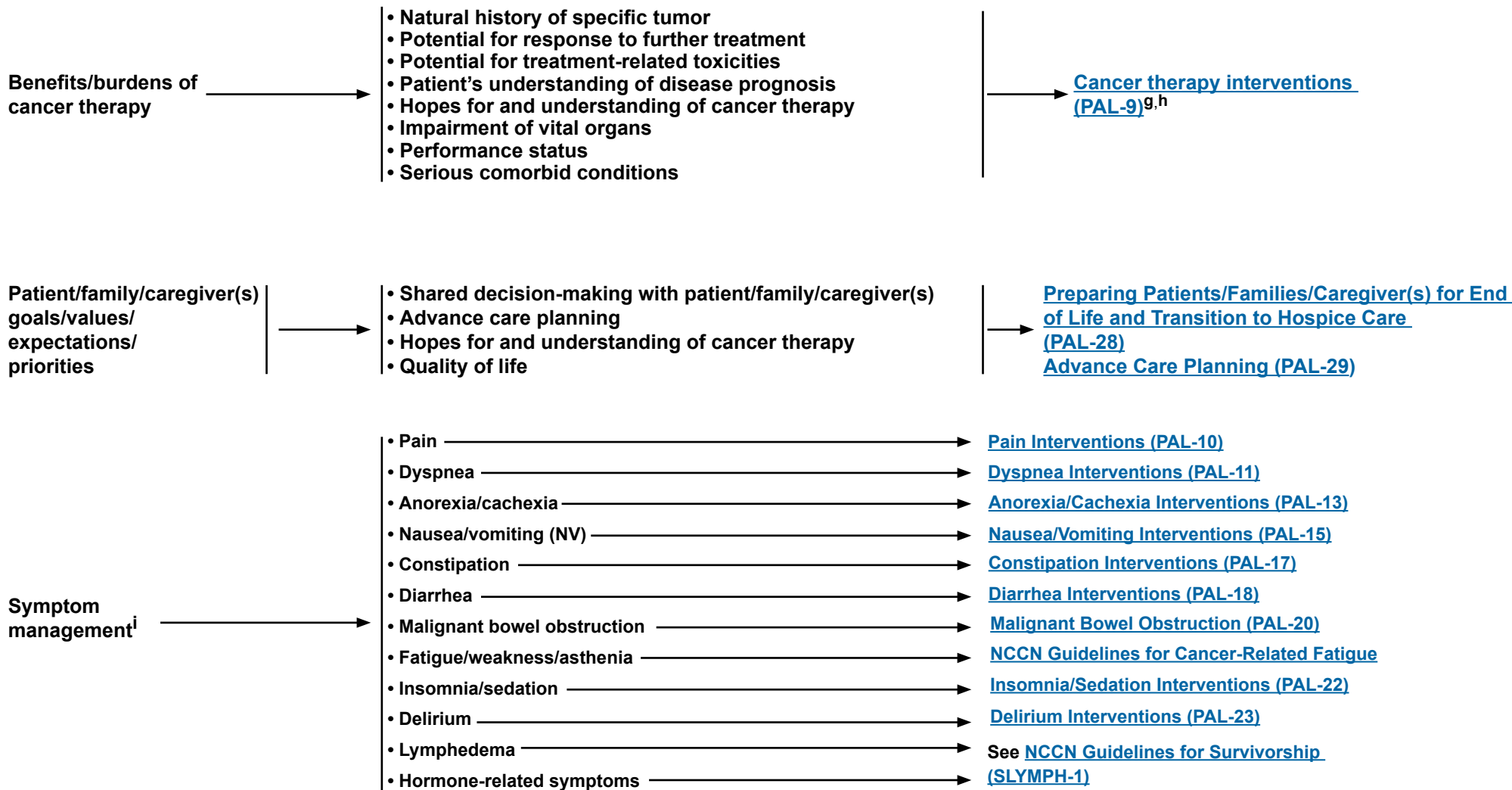
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### ASSESSMENT BY ONCOLOGY TEAM



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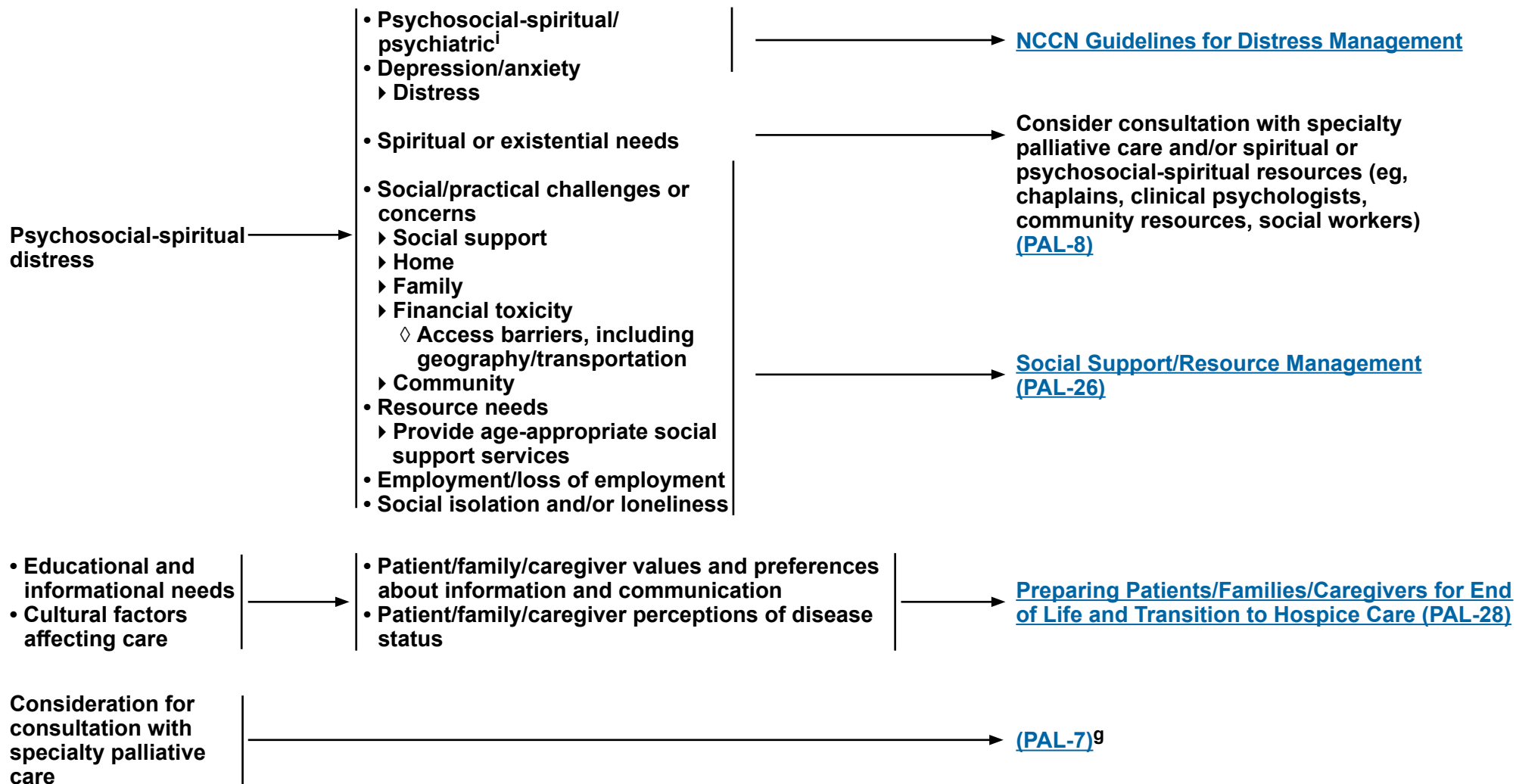
<sup>h</sup> For an approach to decision-making in older adults and geriatric screening tools, see the [NCCN Guidelines for Older Adult Oncology](#).

<sup>i</sup> Look for opportunities to use single agents to treat multiple symptoms.

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### ASSESSMENT BY ONCOLOGY TEAM



<sup>9</sup> See FEV-D in the [NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections](#) for an approach to assess for the risk of serious complications in patients with neutropenic fever.

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### ONCOLOGY TEAM INTERVENTIONS

- Collaborate with palliative care specialist/team<sup>e,f</sup>
- Collaborate with other health care professionals treating the patient
- Evaluate and treat undiagnosed mental health problems
- Consider additional referrals:
  - Mental health
  - Psychosocial-spiritual services
  - Behavioral health
  - Substance use disorders
  - Other specialists
- Mobilize community support
  - Religious
  - School
  - Community agencies
- Introduce advance care planning conversations
- Expedite referral to hospice services when appropriate

### REASSESSMENT

#### Outcomes:

- Adequate symptom management
- Reduction of patient/family/caregiver distress
- Acceptable sense of control
- Decreased caregiver burden
- Strengthened relationships
- Optimized quality of life
- Personal growth and enhanced meaning
- Advance care planning in progress

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

If ongoing needs →

- Re-evaluate intervention options and intensify as possible
- Assess for communication barriers and address as needed (eg, translation services, improved literacy of materials, palliative care)
- Promote adaptive coping.
- See [NCCN Guidelines for Distress Management](#)

Ongoing reassessment

<sup>e</sup> Patients with one or more positive indicators may benefit from a care plan developed by an interprofessional team of physicians, nurses, social workers, mental health professionals, chaplains, advanced practice clinicians, and other health care professionals.

<sup>f</sup> Oncologists should integrate palliative care into general oncology care. Early consultation/collaboration with a specialty palliative care/hospice team should be considered to improve quality of life and survival.

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### CONSIDERATION FOR CONSULTATION WITH SPECIALTY PALLIATIVE CARE

#### ASSESSMENT

Patient characteristics →

- [Assessment by Oncology Team \(PAL-3\)](#)
- Limited cancer treatment options due to:
  - ▶ Limited access to cancer treatment
  - ▶ Disease refractory to cancer treatment
  - ▶ Multiple and/or severe comorbid conditions
  - ▶ Progressive functional decline or persistently poor performance status
- Concerns about decision-making capacity [[NCCN Guidelines for Older Adult Oncology \(OAO-1\)](#)]
- 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-spiritual and/or family distress
  - ▶ Rapid escalation of opioid dose
  - ▶ History of multiple adverse reactions to pain and symptom management interventions
  - ▶ History of diagnosis/suspicion of substance use disorder — Refer to chemical dependency program as needed ([NCCN Guidelines for Adult Cancer Pain](#))
- High non-pain symptom burden, especially those resistant to conventional management (see [PAL-4](#) for symptoms)
- High level of psychological distress based on standardized distress screening ([NCCN Guidelines for Distress Management](#))
- Need for invasive procedures (eg, palliative stenting or venting gastrostomy)
- Frequent emergency department visits or hospital admissions
- Need for intensive care unit (ICU)-level care (especially involving multi-organ system failure or prolonged mechanical support)
- Communication needs
  - ▶ Language
  - ▶ Literacy
  - ▶ Culture
  - ▶ Cognitive impairment
- Patient/family requests consultation
- Request for hastened death

→ [Oncology Team Interventions \(PAL-6\)](#)

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[Continued](#)



### CONSIDERATION FOR CONSULTATION WITH SPECIALTY PALLIATIVE CARE

#### ASSESSMENT

Complex patient/family/caregiver circumstances

- High risk for persistent complicated grief
- Inadequate social support
- Substance use disorder impacting care
- Financial limitations
- Limited access to care
- Family/caregiver discord impacting care
- Spiritual or existential distress
- 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
  - Care planning for children of parent with poor prognosis
  - Support for active caregivers
- Other complexities related to social determinants of health

[Oncology Team Interventions \(PAL-6\)](#)

Oncology care team/staff challenges

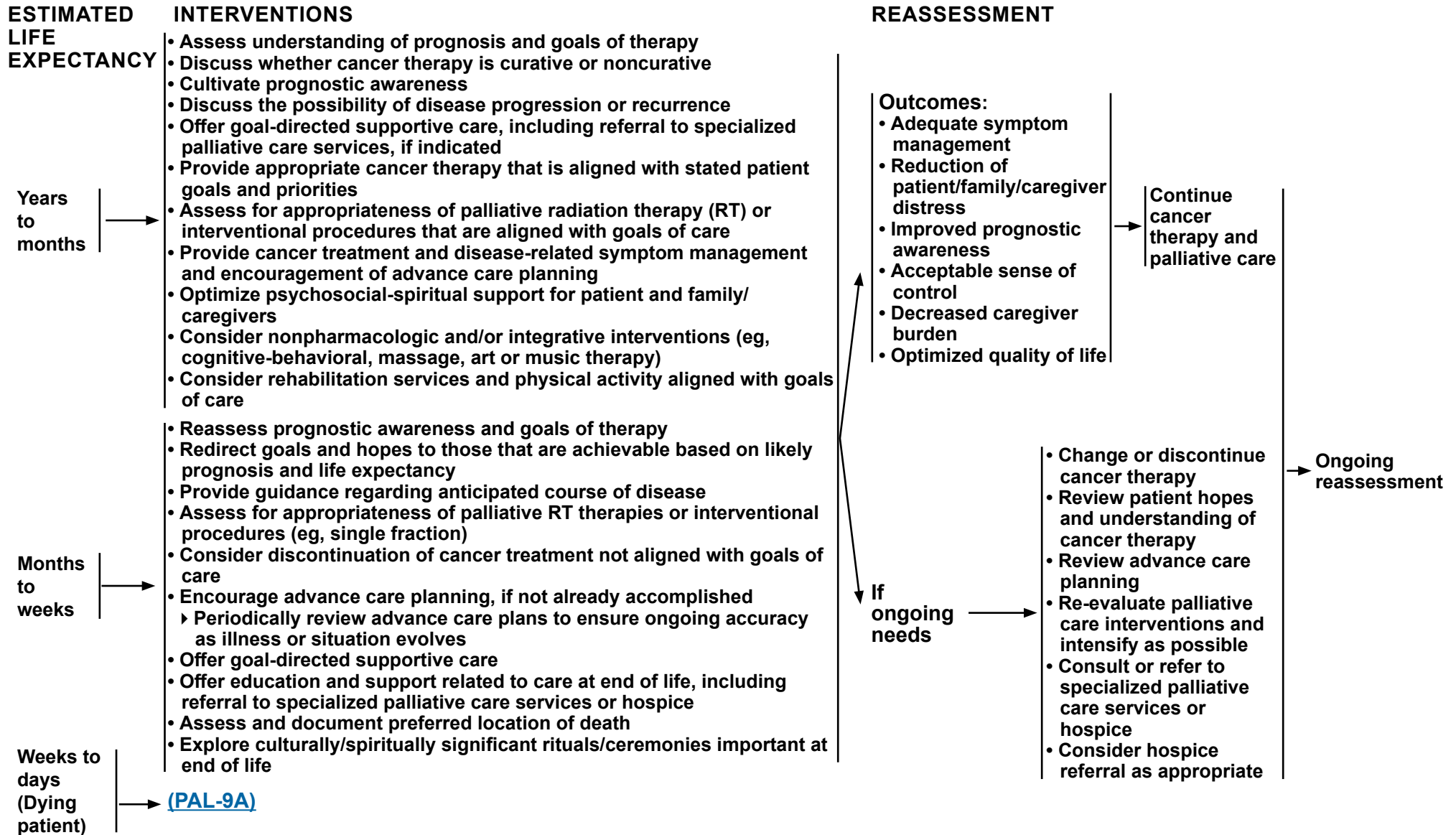
- Complex care coordination issues within and among multiple care teams
- Compromised resilience including:
  - Intra-team or inter-team conflict
  - Compassion fatigue
  - Moral distress and/or ethical concerns
  - Burnout
- Communication surrounding complex decision-making

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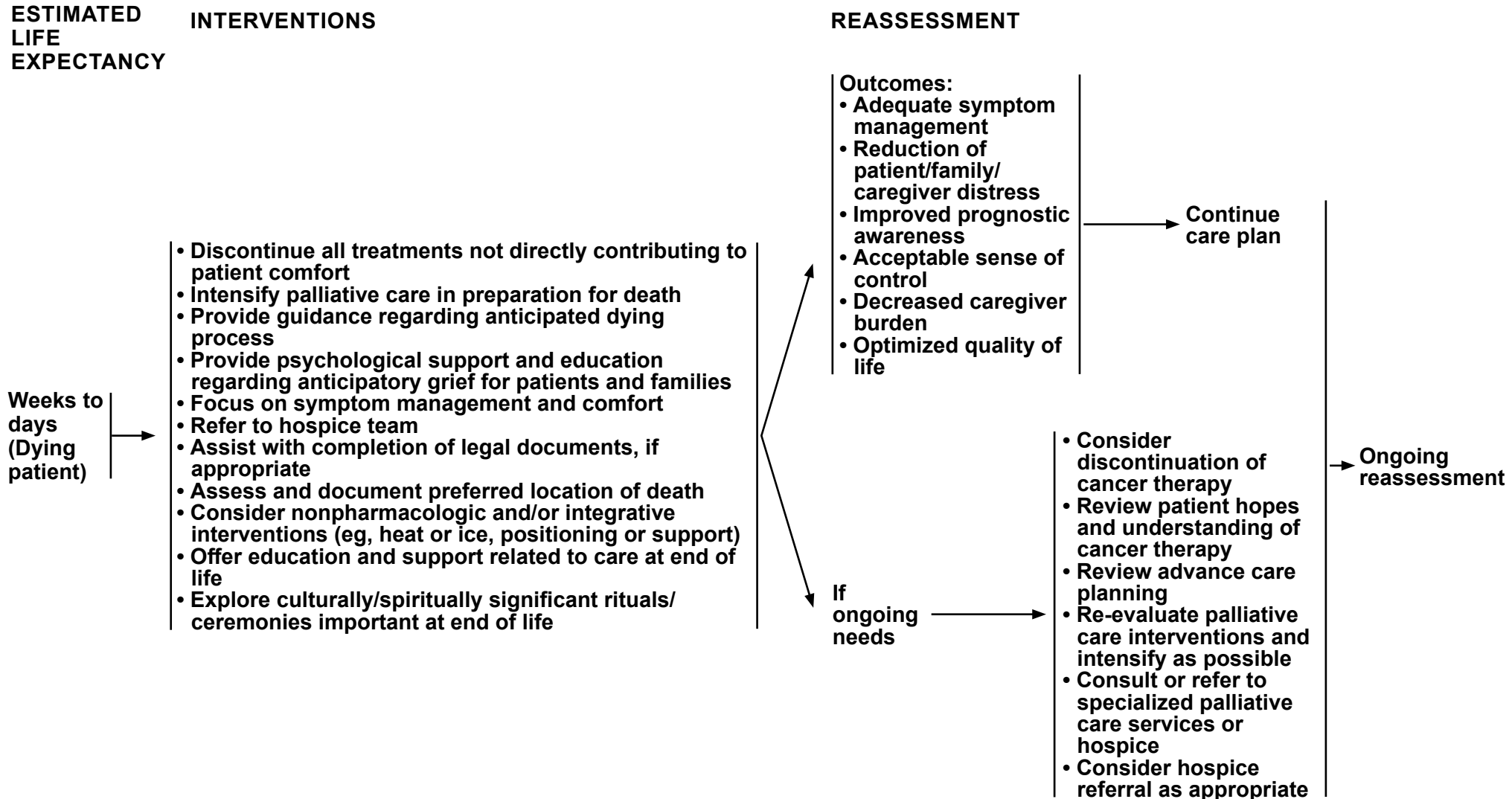
### SHARED DECISION-MAKING CONSIDERATIONS



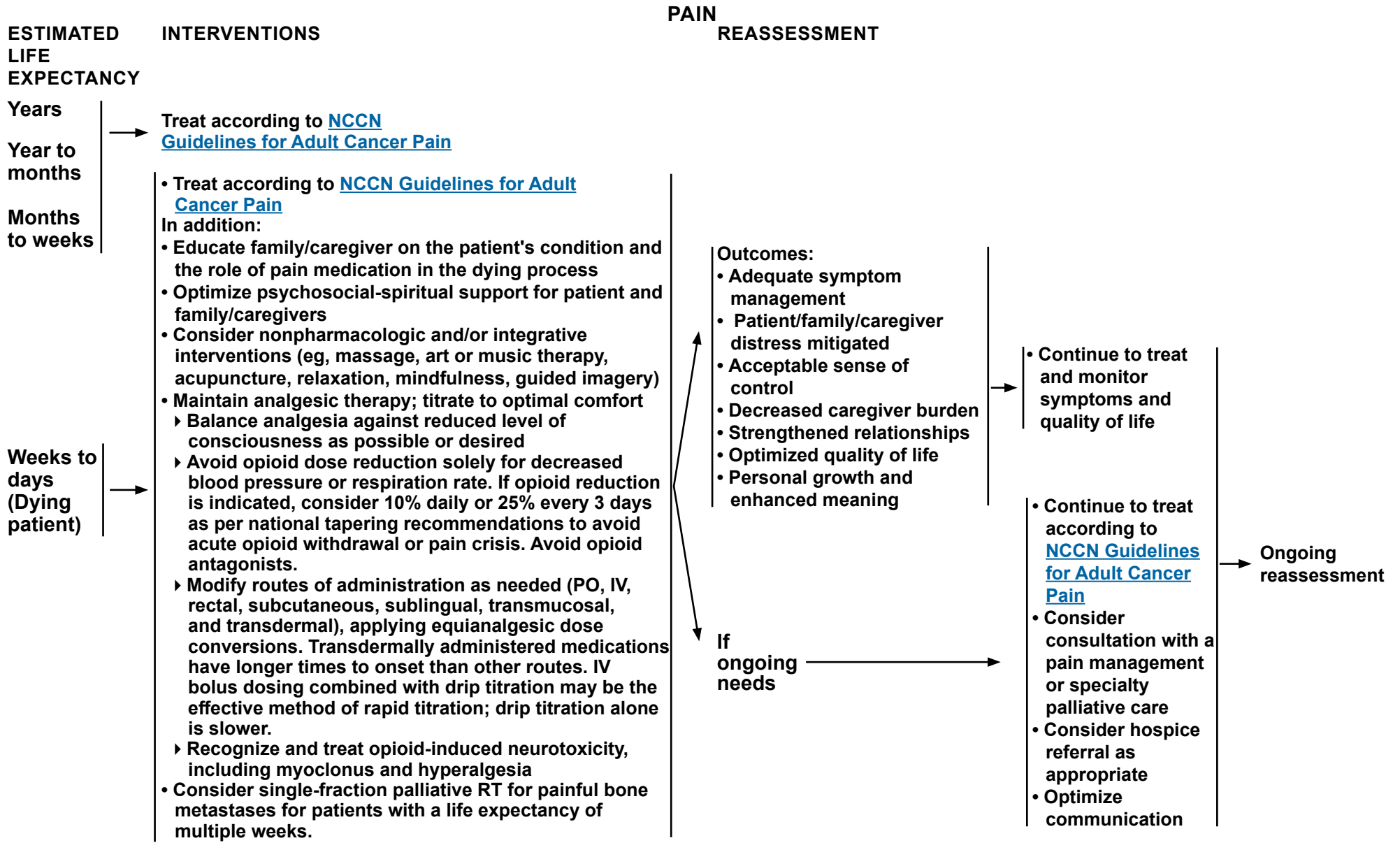
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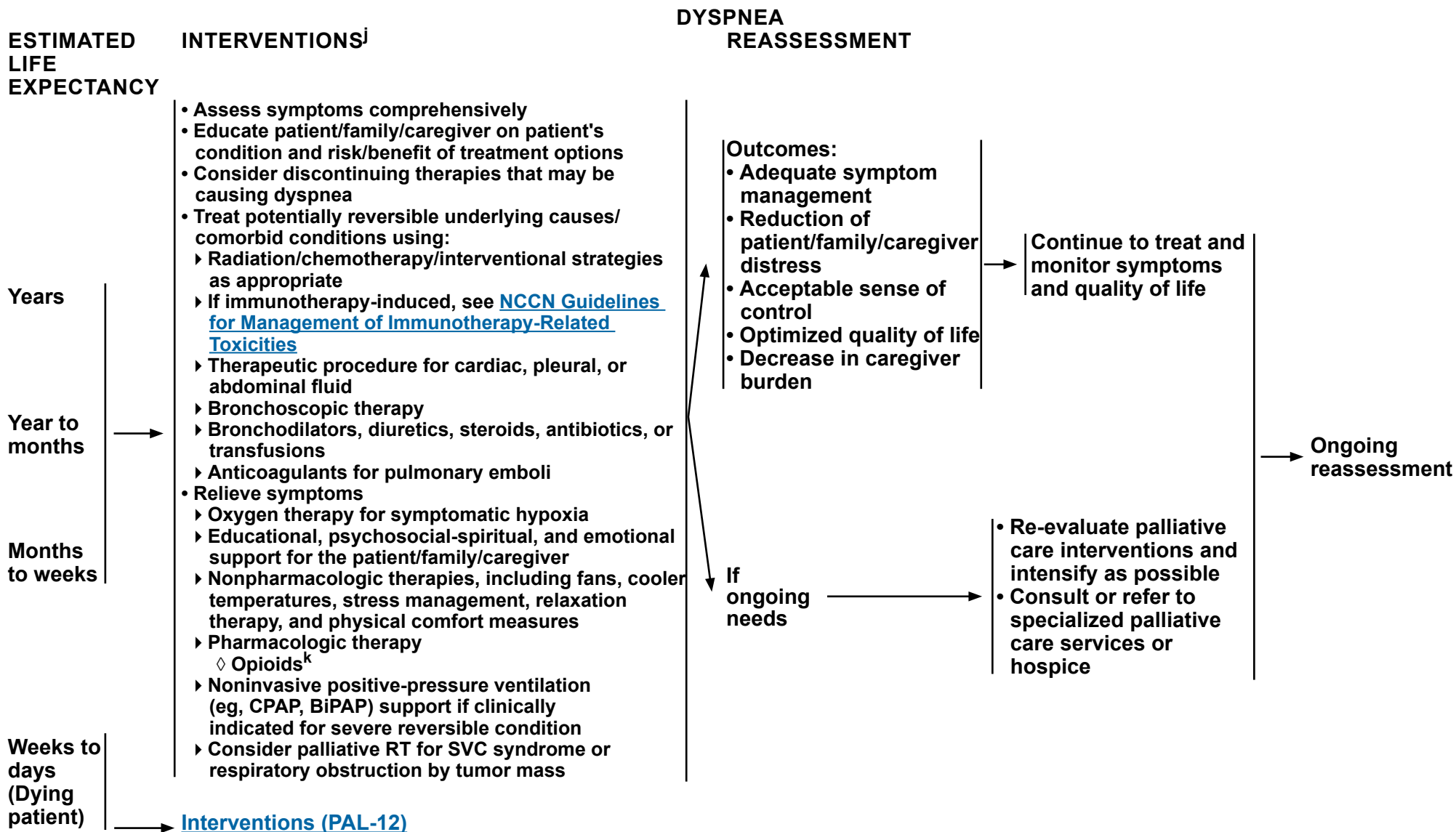


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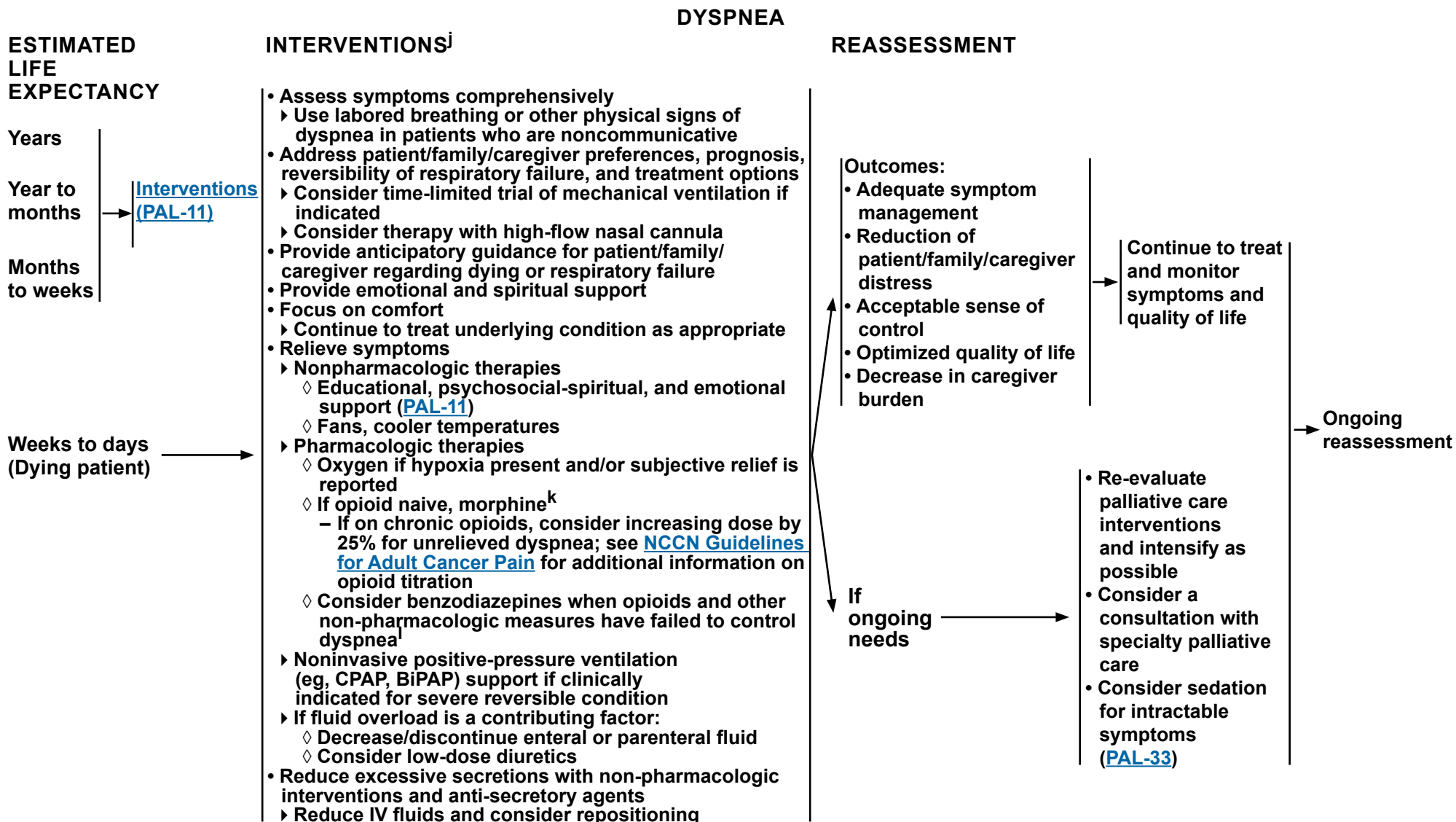




<sup>j</sup> See [Drug Appendix \(PAL-A\)](#) for specific recommendations for medical management of symptoms.

<sup>k</sup> For acute progressive dyspnea or for patients who are opioid tolerant, more aggressive titration may be required.

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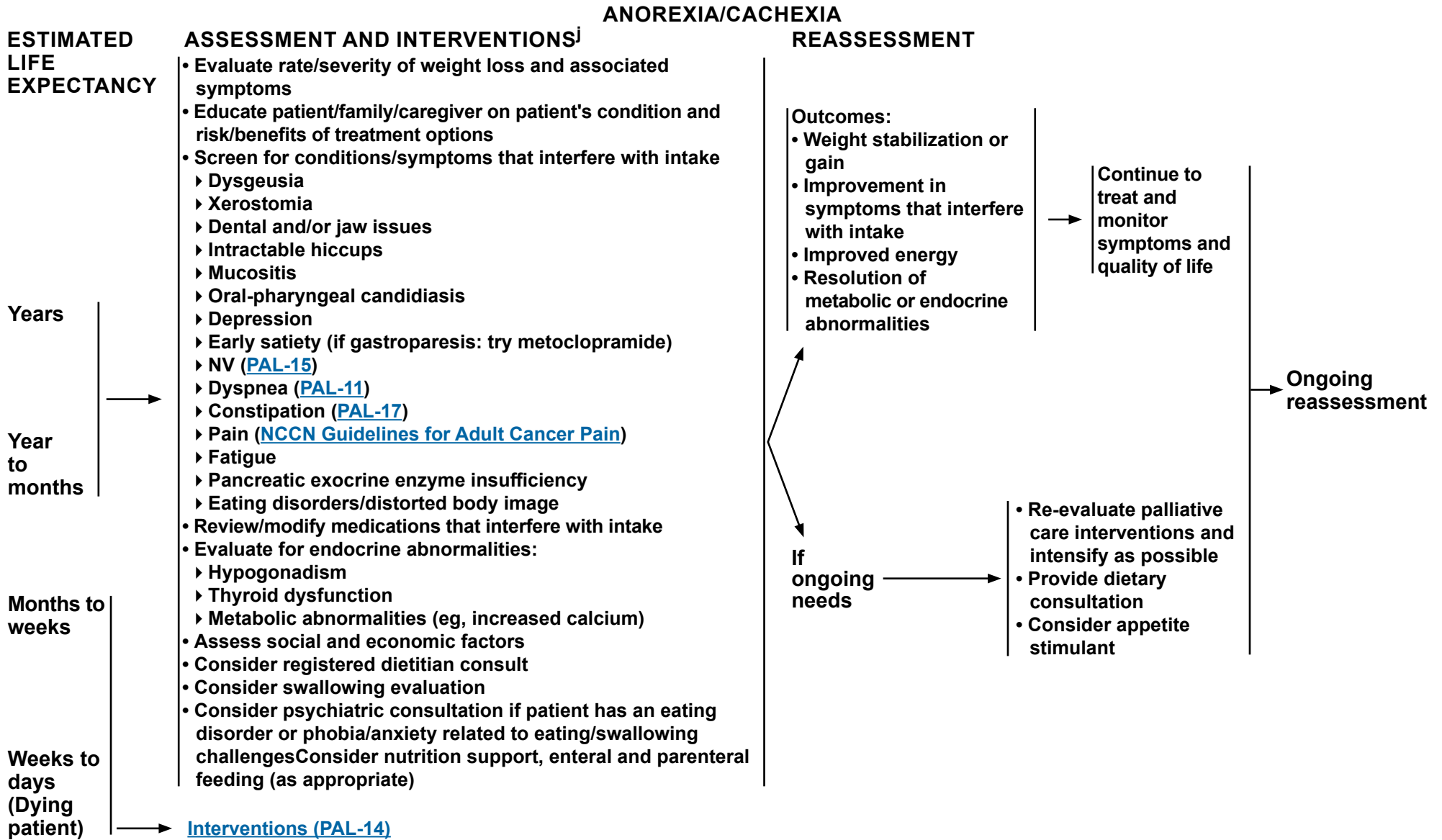


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<sup>l</sup> The addition of benzodiazepines to opioids can increase the risk of respiratory depression.

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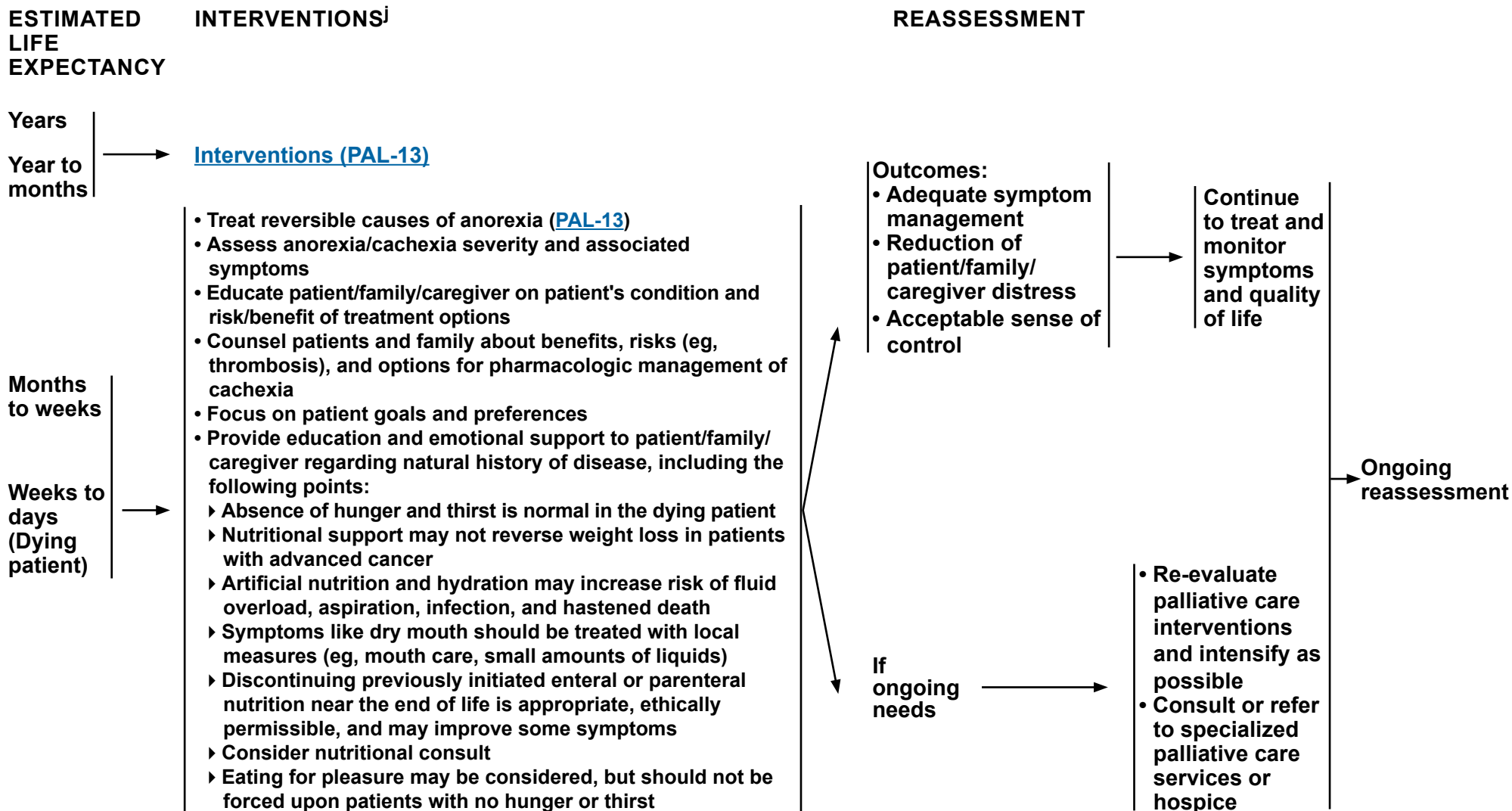


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### ANOREXIA/CACHEXIA



<sup>j</sup> See [Drug Appendix \(PAL-A\)](#) for specific recommendations for medical management of symptoms.

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### INTERVENTIONS<sup>j</sup>

- Assess NV severity and associated symptoms
- Educate patient/family/caregivers on patient's condition and treatment options
- Screen for potentially reversible causes/common etiologies:
  - ▶ Chemotherapy/RT-induced ([NCCN Guidelines for Antiemesis](#))
    - ◇ Acupressure<sup>m</sup>
  - ▶ Severe constipation/fecal impaction ([PAL-17](#))
  - ▶ Gastroparesis
    - ◇ Prokinetic agent
  - ▶ Bowel obstruction ([PAL-20](#))
  - ▶ Central nervous system (CNS) involvement
    - ◇ Corticosteroids
    - ◇ Palliative RT
  - ▶ Gastrointestinal (GI) obstruction from intra-abdominal tumor or liver metastasis
    - ◇ Consider treatment with corticosteroids, a proton pump inhibitor, and metoclopramide<sup>n</sup>
    - ◇ Endoscopic stenting
    - ◇ Decompressing gastrostomy tube (G-tube)
    - ◇ Consider interventional procedures
  - ▶ Gastritis/gastroesophageal reflux disease (GERD)
    - ◇ Proton pump inhibitor
    - ◇ H2-blocker
- Treat dehydration, uremia, and hypercalcemia
  - ▶ Hydrate and optimize electrolytes

### NAUSEA AND VOMITING

- 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 [TCAs])
  - ▶ 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 ([NCCN Guidelines for Distress Management](#))
- Non-specific NV
  - ▶ Initiate pharmacologic management with dopamine receptor antagonists or 5-HT<sub>3</sub> 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 immunotherapy-induced, see [NCCN Guidelines for Management of Immunotherapy-Related Toxicities](#)

If NV stops:  
see [Reassessment \(PAL-16\)](#)

If NV persists:  
see [Interventions \(PAL-16\)](#)

<sup>j</sup> See [Drug Appendix \(PAL-A\)](#) for specific recommendations for medical management of symptoms.

<sup>m</sup> Lyman GH, et al. J Clin Oncol 2018;36:2647-2655.

<sup>n</sup> Do not give metoclopramide in patients with complete gastric outlet obstruction.

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### PERSISTENT NAUSEA AND VOMITING

#### INTERVENTIONS<sup>j,o,p</sup>

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

#### REASSESSMENT

- Outcomes:
- Adequate 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

If ongoing needs

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

Ongoing reassessment ([Interventions, PAL-15](#))

<sup>j</sup> [Drug Appendix \(PAL-A\)](#) for specific recommendations for medical management of symptoms.

<sup>o</sup> An around-the-clock dosing schedule may provide the most consistent benefit to the patient.

<sup>p</sup> Continuous intravenous or subcutaneous infusions of different antiemetics may be necessary for the management of intractable NV.

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### CONSTIPATION<sup>r,s</sup>

#### INTERVENTIONS<sup>j</sup>

- 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 examination, abdominal x-ray/consider GI consult)
  - Treat other causes (eg, hypercalcemia, hypokalemia, hypothyroidism, diabetes mellitus, medications, side effects of immunotherapy)
  - Add and titrate stimulant and/or osmotic laxative If impacted:
    - Administer glycerin suppository ± mineral oil retention enema<sup>q</sup>
    - Perform manual disimpaction following pre-medication with analgesic ± anxiolytic
  - If constipation persists:**
    - Reassess for cause and severity of constipation
    - Recheck for impaction or obstruction
    - Titrate laxative agents to achieve desired frequency Consider peripherally acting mu-opioid receptor antagonist (PAMORA) or secretory agents for opioid-induced constipation
      - When two medications scheduled from different laxative classes have been ineffective
      - Avoid if concern for postoperative ileus and/or mechanical bowel obstruction
    - Administer enema until clear: eg, tap water, soap suds, mineral oil, lactulose

- Preventive measures<sup>j</sup>**
- 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 one non-forced bowel movement every 1–2 days

#### REASSESSMENT

- Outcomes:**
- Adequate symptom management
  - Reduction of patient/family/caregiver distress

Continue to treat and monitor symptoms and quality of life

If ongoing needs

- Re-evaluate palliative care interventions and intensify as possible
- Consider referral to GI specialist
- Consider referral to specialized palliative care services or hospice

Ongoing reassessment

<sup>j</sup> See [Drug Appendix \(PAL-A\)](#) for specific recommendations for medical management of symptoms.

<sup>q</sup> Use suppository and enema with caution in patients receiving chemotherapy due to risk of cytopenia.

<sup>r</sup> Wickham RJ. J Adv Pract Oncol 2017;8:149-161.

<sup>s</sup> Larkin PJ, et al. Ann Oncol 2018;29(Suppl 4):iv111-iv125.

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### DIARRHEA

#### SCREENING AND ASSESSMENT

- Evaluate diarrhea severity and potential causes
- Educate patient/family/caregiver on condition and treatment options

#### Determine Diarrhea Severity/Grade<sup>t</sup>

- **Mild/Grade 1:** Increase of <4 stools/day over baseline; mild increase in ostomy<sup>u</sup> output
- **Moderate/Grade 2:** Increase of 4–6 stools/day over baseline; moderate increase in ostomy output<sup>v</sup>
- **Severe/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)<sup>w</sup>
- **Severe/Grade 4:** Life-threatening consequences; urgent intervention indicated<sup>w</sup>

#### INTERVENTIONS

- Tailor treatment to potential causes
  - ▶ If immunotherapy-induced, see [NCCN Guidelines for Management of Immunotherapy-Related Toxicities](#)
  - ▶ Graft-versus-host disease (GVHD) and/or immunotherapy-related colitis
  - ▶ Chemotherapy regimen
  - ▶ Radiation-induced enteritis or other RT side effects
  - ▶ Infection
    - ◊ Screen for Clostridioides difficile (C. diff), HIV, and other comorbid infections (ie, ova/parasites)
  - ▶ Drugs that frequently induce diarrhea
  - ▶ Dietary changes
  - ▶ Post-surgical/anatomic changes (ie, short bowel syndrome)
  - ▶ Pancreatic insufficiency in pancreatic cancer
  - ▶ Irritable bowel syndrome (IBS)/Crohn's disease
  - ▶ Recent antibiotic use
- If fecal impaction is suspected, see [PAL-17](#)
- Provide immediate antidiarrheal therapy indicated by grade
- If chemotherapy induced, decrease or delay the next dose of chemotherapy
- Consider endoscopy if diagnostic uncertainty

See Anti-Diarrheal Interventions, Grades 1–4 ([PAL-19](#))

<sup>t</sup> [National Cancer Institute's Common Terminology Criteria for Adverse Events: Diarrhea.](#)

<sup>u</sup> Euvolemic and no electrolyte abnormalities.

<sup>v</sup> Hypovolemia plus/minus electrolyte abnormalities.

<sup>w</sup> Severe hypovolemia and/or electrolyte abnormalities.

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### ANTIDIARRHEAL INTERVENTIONS

#### ASSESSMENT

#### INTERVENTION<sup>j</sup>

Any Grade

- Treat underlying cause as appropriate
- If chemotherapy induced, decrease or delay the next dose of chemotherapy
- If immunotherapy-induced diarrhea, see [NCCN Guidelines for Management of Immunotherapy-Related Toxicities](#)
- For GVHD diarrhea, consider limiting diet, steroids, and IV nutrition
- Provide oral hydration and electrolyte replacement
- Provide IV fluids and hydration if patient is unable to tolerate oral fluids

Mild/Grade 1

- Consider antidiarrheal agents (eg, loperamide) if infection ruled out
- If IBS-related, utilize cognitive behavioral interventions complementary to medication interventions<sup>x</sup>

Moderate/Grade 2

- Provide IV fluids if patient is unable to tolerate oral fluids
- Initiate/continue antidiarrheal agents—as above if infection ruled out
- Consider anticholinergic agents
- If non-C. diff infection-related, treat with appropriate antibiotics
- If C. diff infection-related, administer antibiotics and probiotics as appropriate

Severe/Grades 3/4

- Inpatient hospitalization (intensive care for Grade 4 if consistent with goals)
- Provide IV fluids and use antidiarrheal agents and anticholinergics as mentioned above
- Consider somatostatin analog
- Consider parenteral hydration in home setting

<sup>j</sup> See Drug Appendix ([PAL-A](#)) for specific recommendations for medical management of symptoms.

<sup>x</sup> Radziwon CD, et al. Curr Gastroenterol Rep 2017;19:49.

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### MALIGNANT BOWEL OBSTRUCTION<sup>y</sup>

#### ESTIMATED LIFE EXPECTANCY

#### ASSESSMENT

Years

Year to  
months

- Evaluate severity and cause(s) of malignant bowel obstruction
- Educate patient/family/caregivers on patient's condition and treatment options
- Screen for and treat underlying potentially reversible causes
  - Adhesions
  - Radiation-induced strictures
  - Internal hernias
- Assess for malignant causes
  - Tumor mass
  - Carcinomatosis
- Consider patient goals, prognosis (including life span post procedure), and relative invasiveness of proposed intervention

[Procedural  
Interventions  
\(PAL-21\)](#)

Months  
to weeks

Weeks to  
days  
(Dying  
patient)

- Consider medical management rather than surgical management
- Assess patient's goals for treatment to guide choice of intervention<sup>z</sup> (eg, decrease NV, support the desire to eat, decrease pain, support patient to go home/to hospice)
- Provide education and support to patient/family/caregiver

- Pharmacologic management
- Intravenous or subcutaneous fluids
- Enteral tube drainage
  - Consider only if other measures fail to reduce vomiting
- Endoscopic management

[\(PAL-21\)](#)

<sup>y</sup> 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.

<sup>z</sup> Most malignant bowel obstructions are partial, allowing time to discuss appropriate intervention with the patient/family/caregiver.

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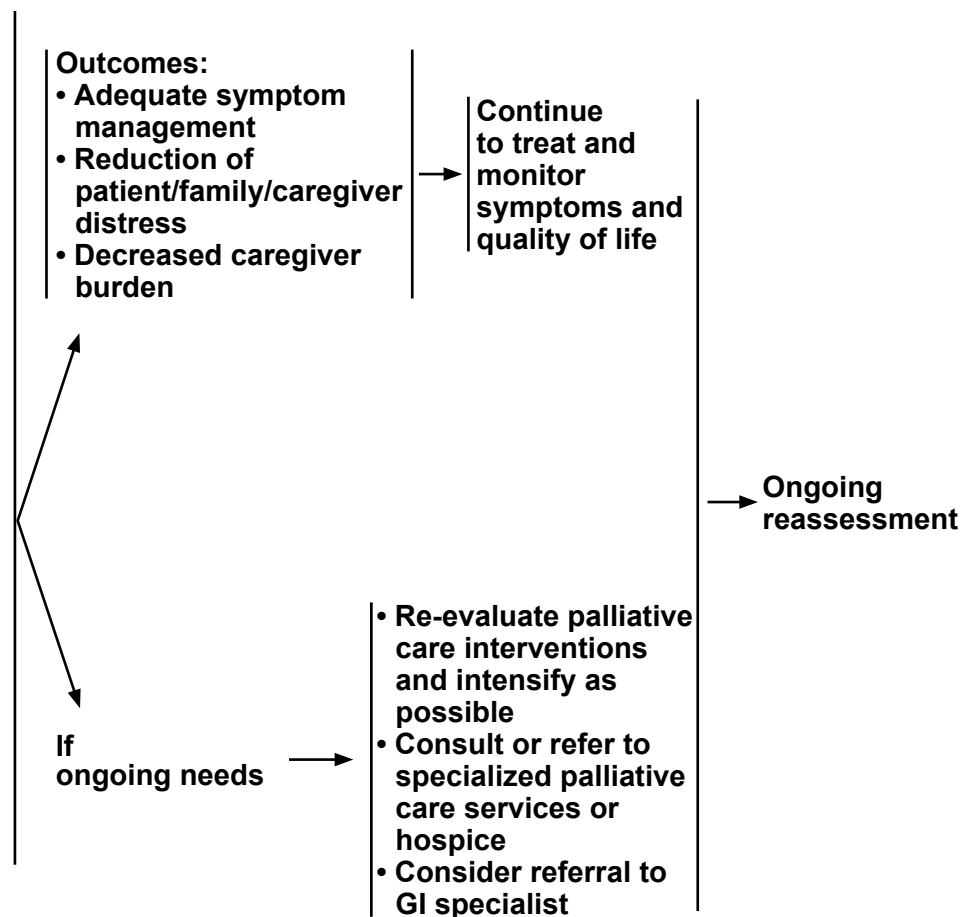


### MALIGNANT BOWEL OBSTRUCTION

#### PROCEDURAL INTERVENTIONS<sup>j</sup>

- Operative management (eg, resection, bypass, diverting ostomy)
  - ▶ 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 (eg, G-tube for drainage, endoscopic stent placement)
- Interventional radiology management
- 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 GI motility such as metoclopramide; however, these may be beneficial in incomplete bowel obstruction
  - ▶ Corticosteroids
- Pharmacologic management when gut function cannot be maintained:
  - ▶ Administer antisecretory agents
  - ▶ Administer intravenous or subcutaneous fluids
- Nasogastric or gastric tube drainage
- Total parenteral nutrition (TPN)
  - ▶ Consider if there is expected improvement in quality of life and life expectancy of months to years

#### REASSESSMENT

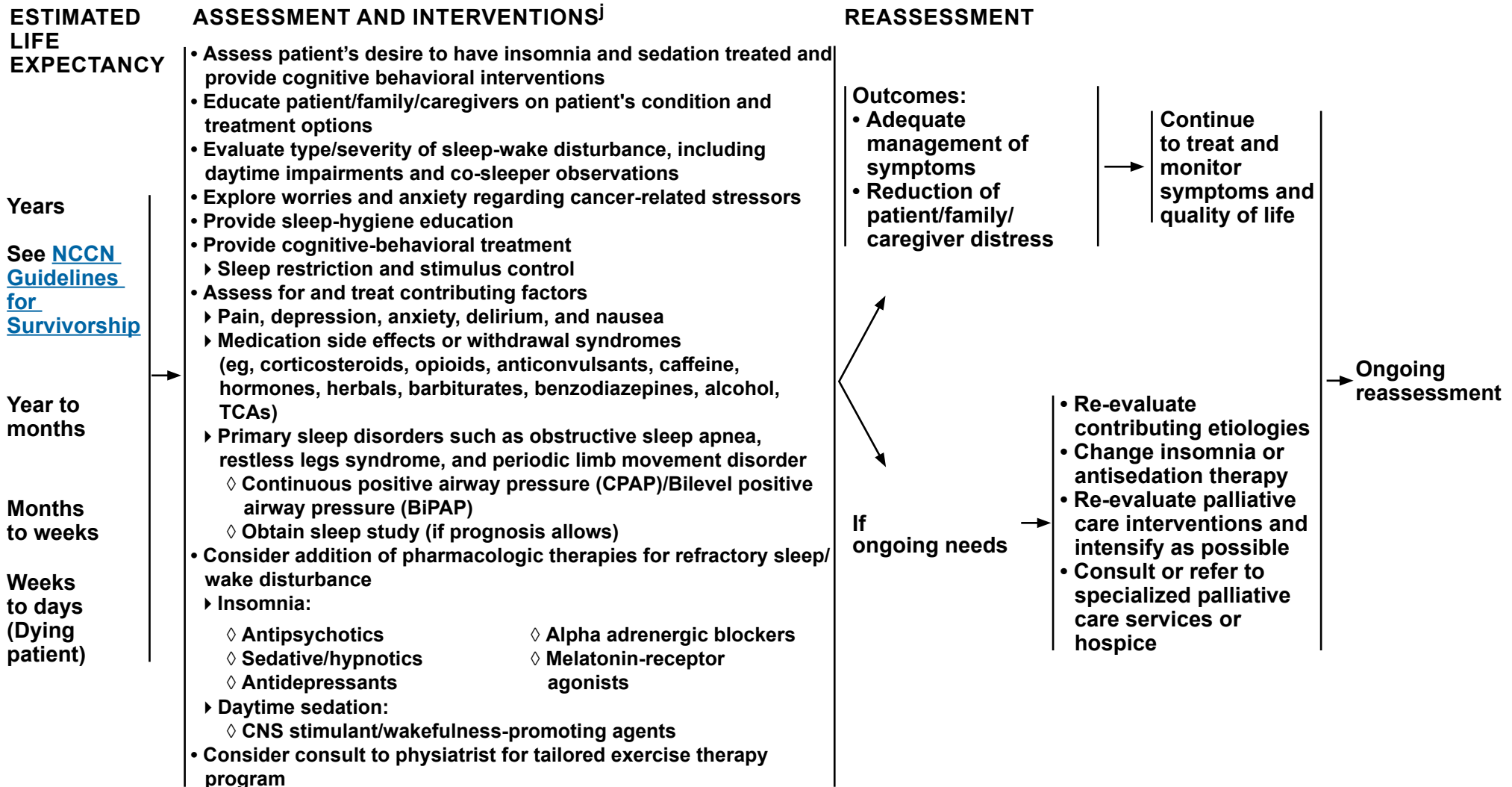


<sup>j</sup> See [Drug Appendix \(PAL-A\)](#) for specific recommendations for medical management of symptoms.

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### SLEEP/WAKE DISTURBANCES INCLUDING INSOMNIA AND SEDATION



<sup>j</sup> See [Drug Appendix \(PAL-A\)](#) for specific recommendations for medical management of symptoms.

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### ESTIMATED LIFE EXPECTANCY ASSESSMENT

- Evaluate delirium severity and cause (eg, DSM criteria)<sup>aa</sup>  
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
  - 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)

Years  
Year to months  
Months to weeks

Weeks to days (Dying patient) → [Interventions \(PAL-24\)](#)

### DELIRIUM INTERVENTIONS<sup>j</sup>

- Reduce or eliminate delirium-inducing medications as possible (eg, steroids, anticholinergics, benzodiazepines)
  - Maximize nonpharmacologic interventions (optimize sleep wake cycle; address sensory impairment; provide glasses, hearing aids)
  - Consider addition of low dose benzodiazepines with or without antipsychotic medications if agitation is severe and either disrupting care or causing the patient distress
  - Titrate starting dose to optimal effect with lowest possible dose
  - Consider opioid dose reduction or rotation
  - Encourage supportive caregiver presence at bedside
  - Support caregivers
- Severe delirium (agitation) →
- Reduce or eliminate delirium-inducing medications as possible
  - Maximize nonpharmacologic interventions
  - Orient patient with family/caregiver(s) presence
  - Support caregivers
- Mild/moderate delirium →

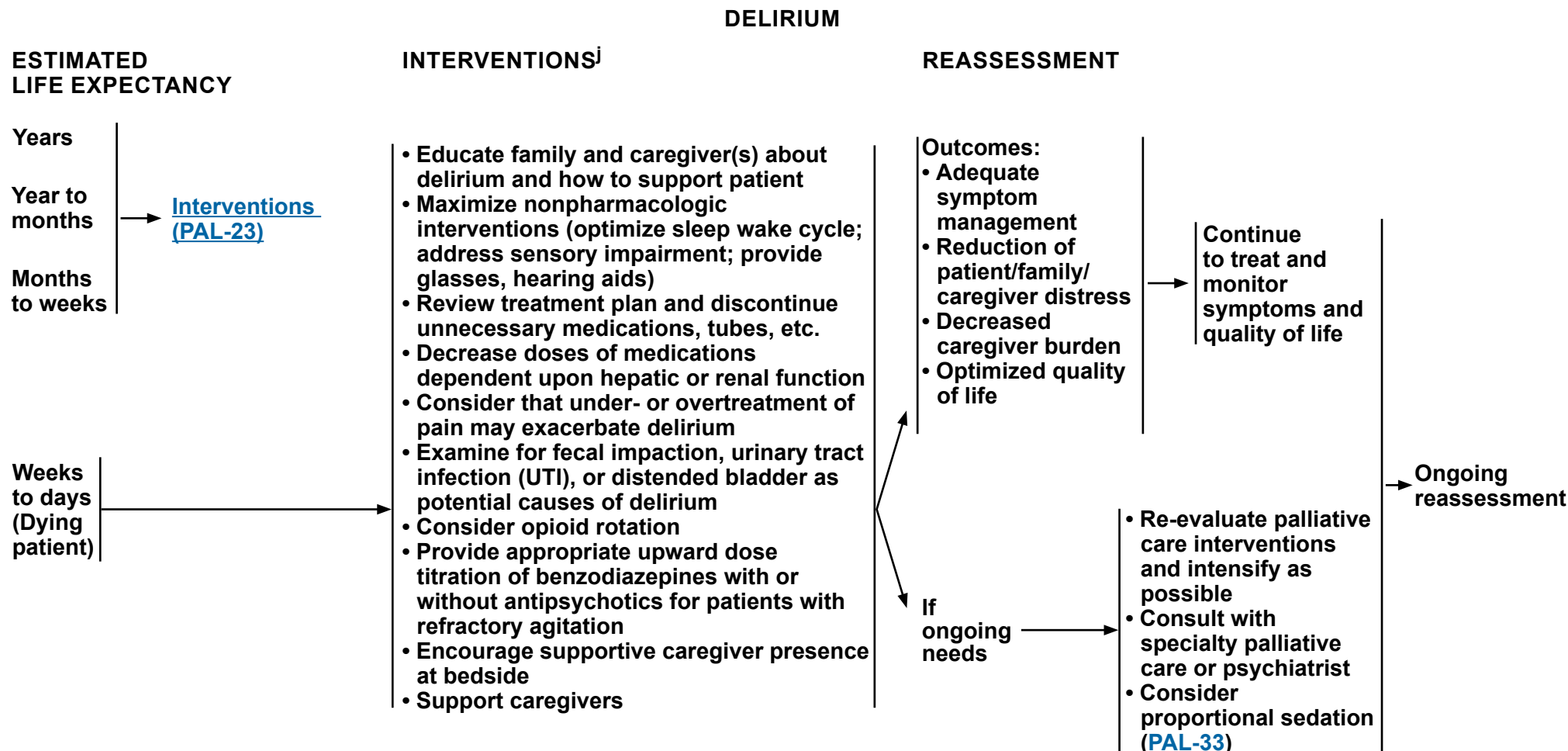
### REASSESSMENT

- Outcomes:
- Adequate symptom management
  - Reduction of patient/family/caregiver distress
  - Decreased caregiver burden
- Continue to treat and monitor symptoms and quality of life
- If ongoing needs →
- Re-evaluate palliative care interventions and intensify as possible
  - Consider consultation with specialty palliative care or psychiatrist

Ongoing reassessment

<sup>j</sup> See [Drug Appendix \(PAL-A\)](#) for specific recommendations for medical management of symptoms.  
<sup>aa</sup> American Psychiatric Association. Diagnostic and statistical manual of mental disorders (ed 5). Arlington, VA: American Psychiatric Publishing; 2013.

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<sup>j</sup> See [Drug Appendix \(PAL-A\)](#) for specific recommendations for medical management of symptoms.

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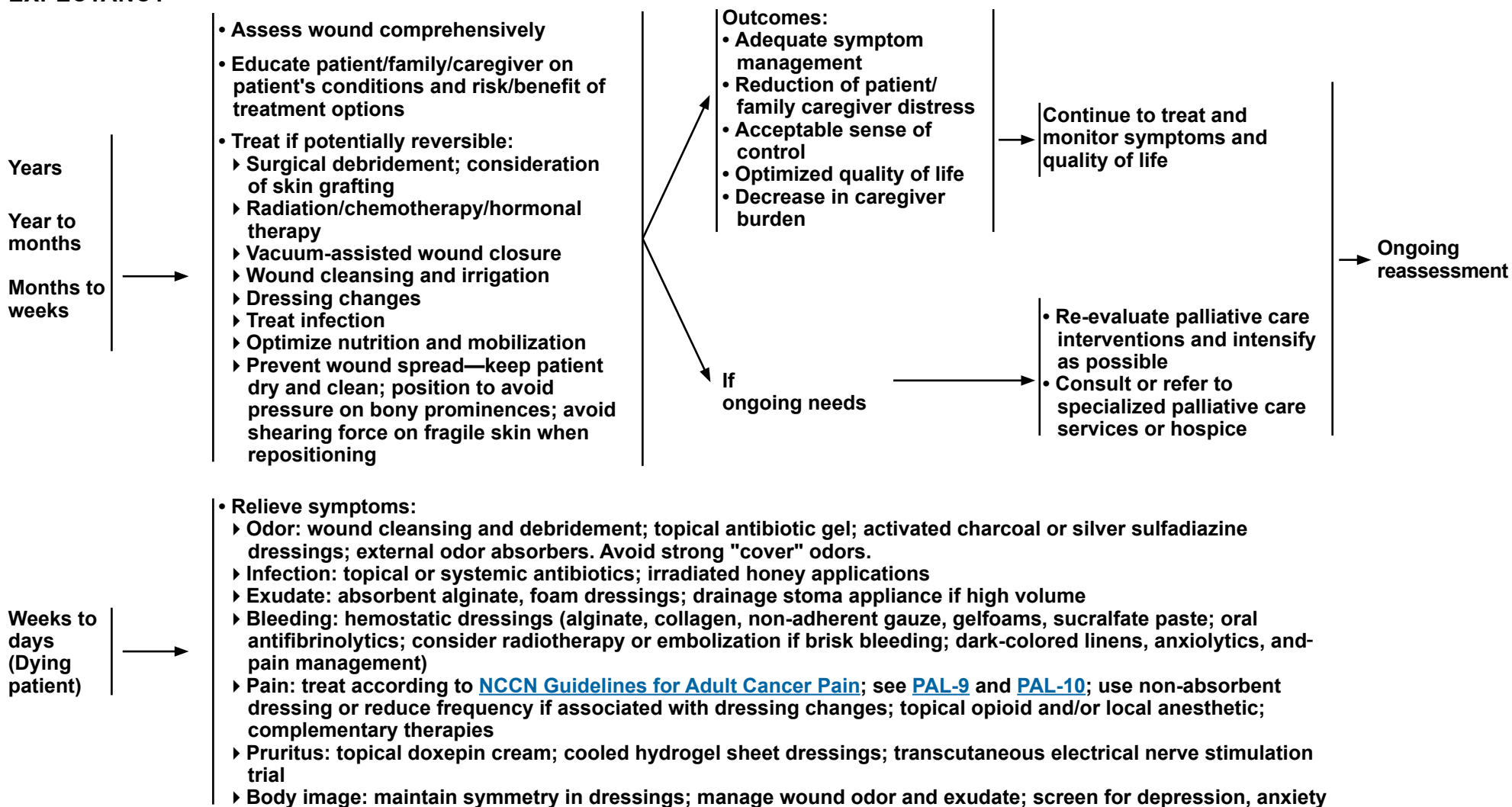


### MALIGNANT WOUNDS

#### ESTIMATED LIFE EXPECTANCY

#### INTERVENTIONS

#### REASSESSMENT

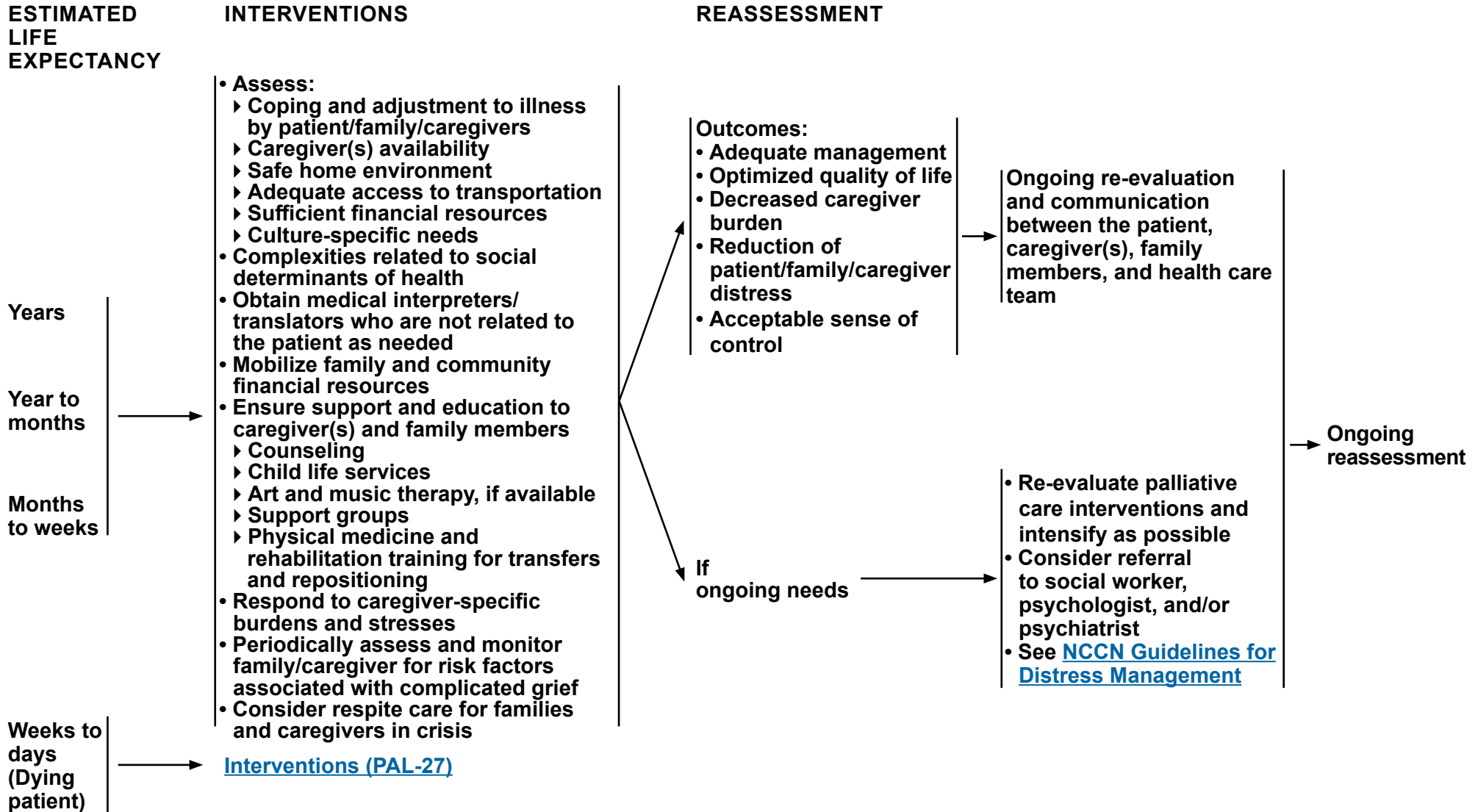


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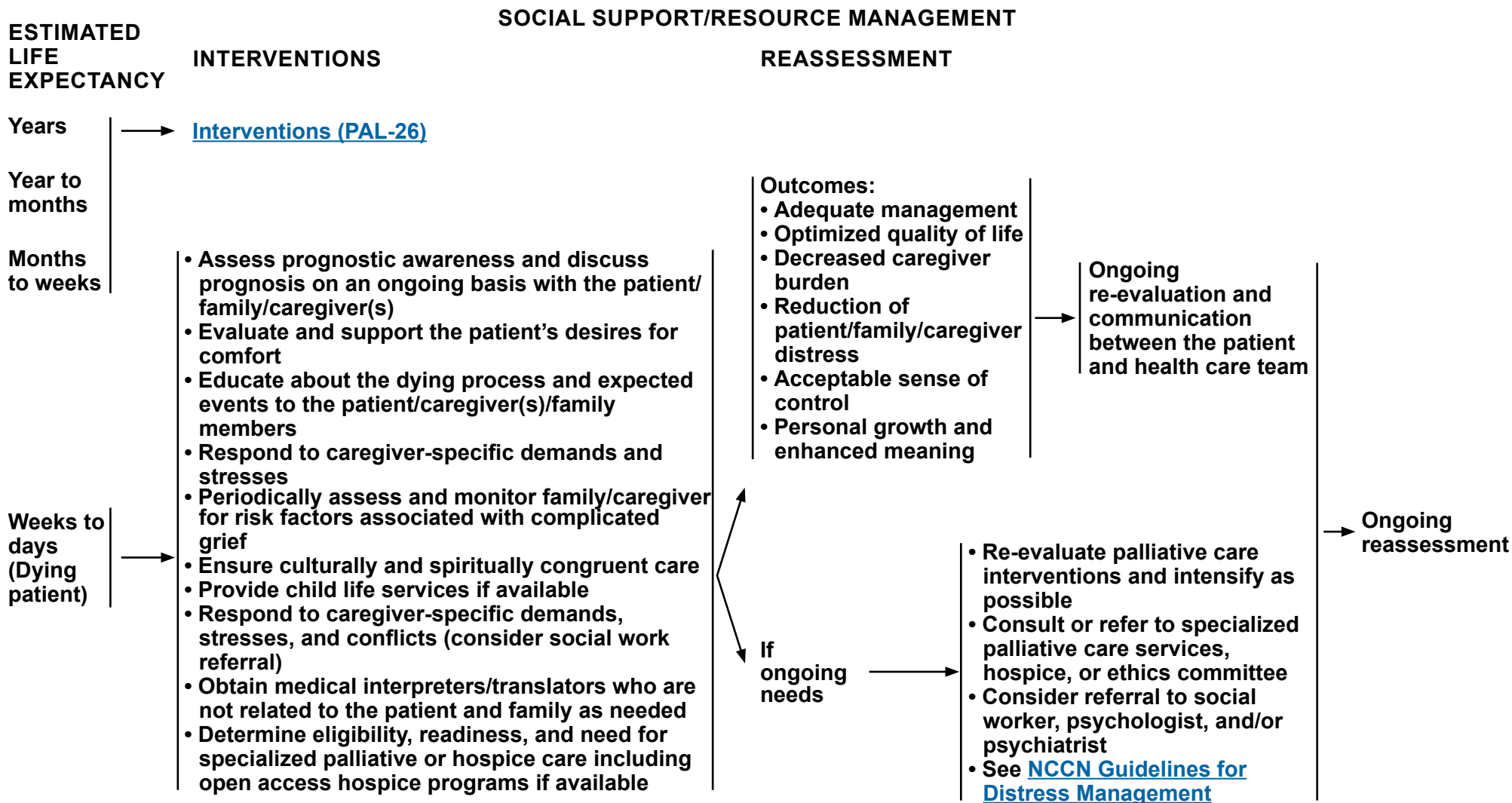


### SOCIAL SUPPORT/RESOURCE MANAGEMENT



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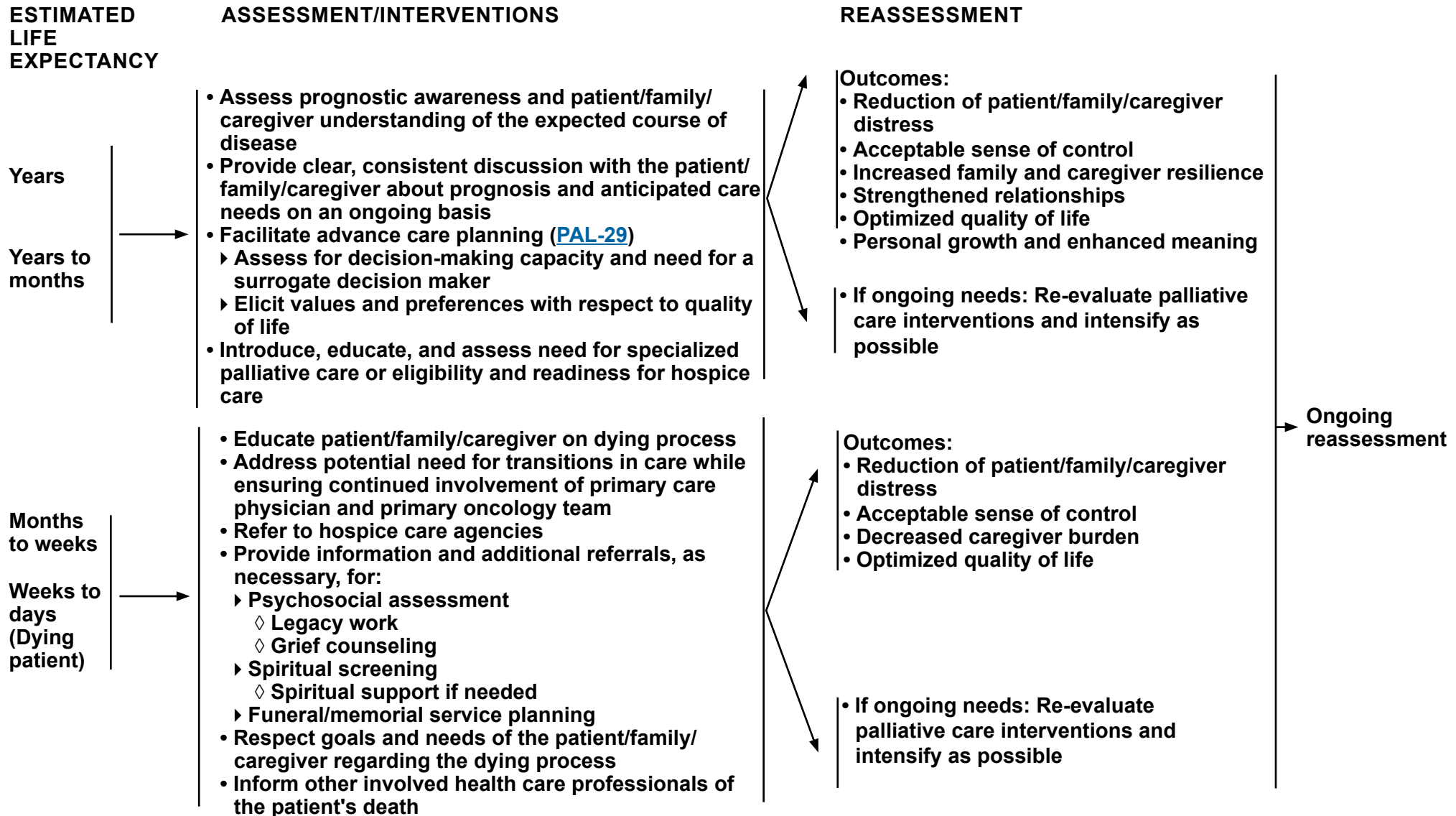


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### PREPARING PATIENTS/FAMILIES/CAREGIVERS FOR END OF LIFE AND TRANSITION TO HOSPICE CARE



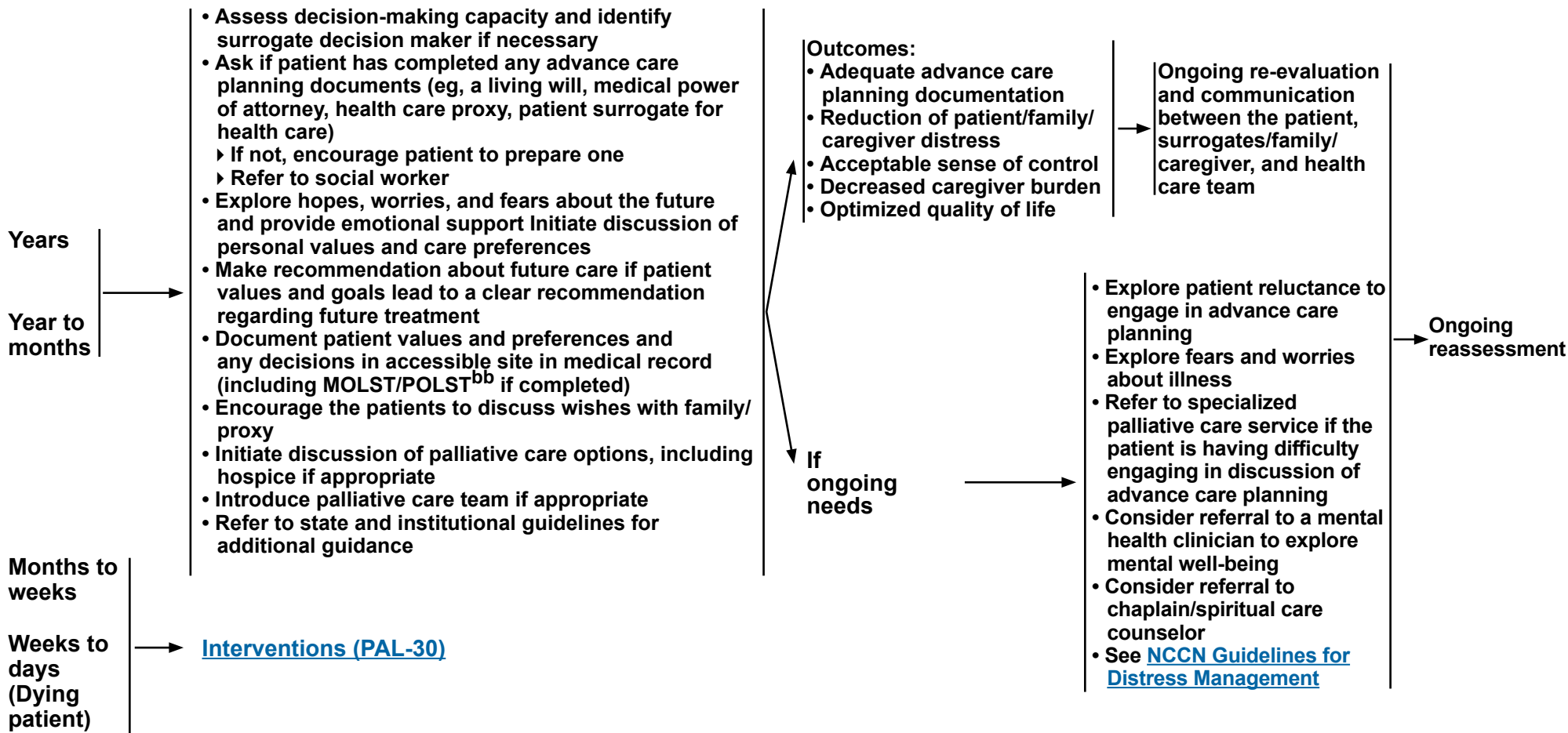
**Note:** All recommendations are category 2A unless otherwise indicated.  
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### ADVANCE CARE PLANNING REASSESSMENT

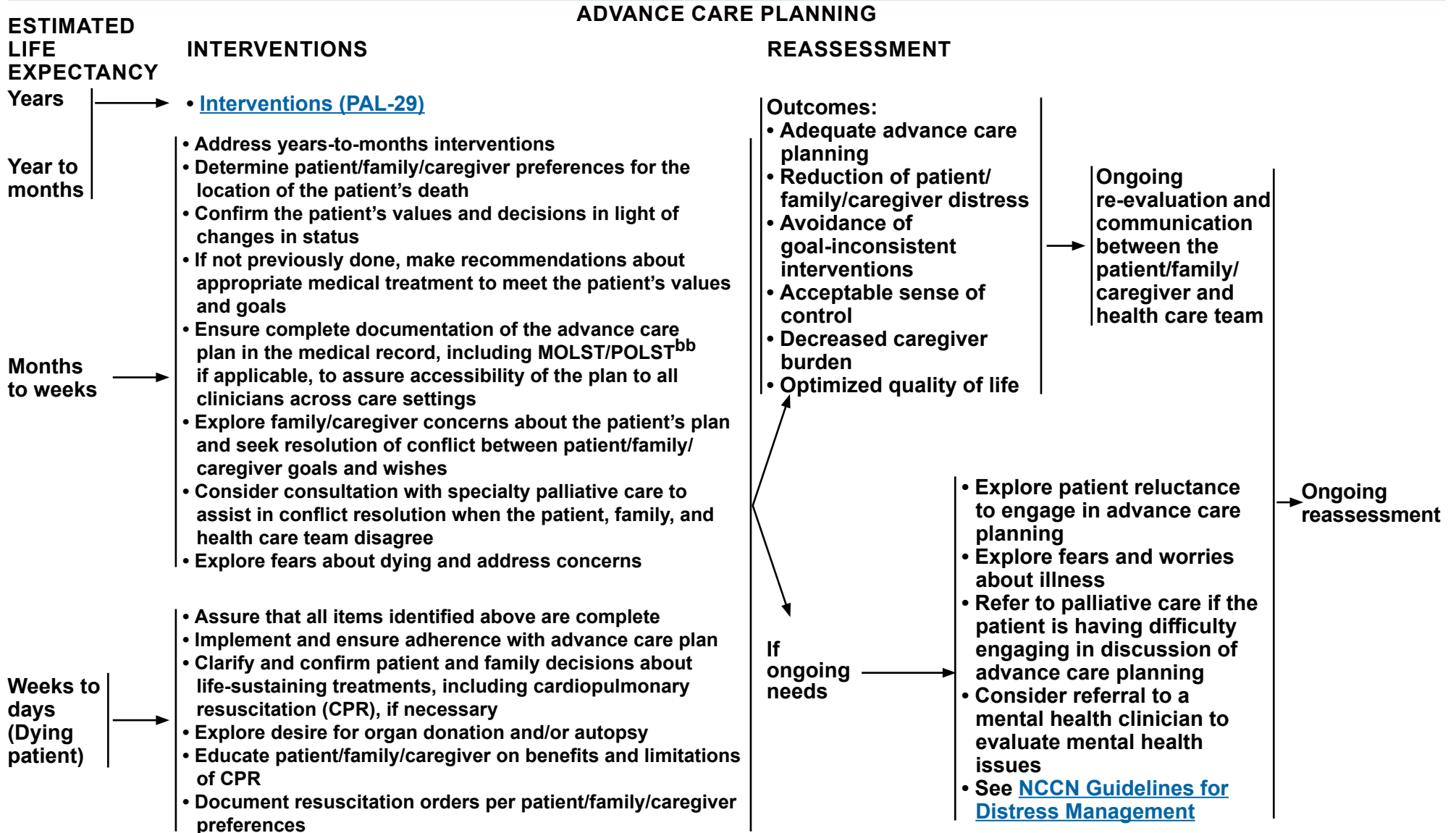
#### ESTIMATED LIFE EXPECTANCY

#### INTERVENTIONS



<sup>bb</sup> 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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<sup>bb</sup> Patient's values and preferences and any decisions should be documented in the medical record, including MOLST/POLST.

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**RESPONSE TO REQUESTS FOR HASTENED DEATH**

- 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 ensure palliative care needs are being met. Patients making such a request may be referred to specialty palliative care. However, evaluating a patient's request for hastened death is an important skill, even for clinicians who feel medical aid in dying (MAID) 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, purpose and meaning, and personal views of spiritual/existential suffering and consider spiritual care consultation for further exploration and intervention.
  - ▶ Assess for worries about 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.
- Consider 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 and local health system policies and procedures of MAID. Some patients and clinicians may be confused about legal/ethical distinctions; treatment withdrawal and aggressive treatments for symptoms, such as pain, are not requests for hastened death.<sup>cc</sup>
- 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 and psychosocial-spiritual distress. Re-emphasize your own commitment to providing continuing care for the patient. Re-evaluate and maintain medications for symptom management.

<sup>cc</sup> Spence RA, J Oncol Pract 2017;13:693-699.**Note: All recommendations are category 2A unless otherwise indicated.****Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.**

**SHARED DECISION-MAKING IN THE CARE OF THE IMMINENTLY DYING HOSPITALIZED PATIENT**

For an imminently dying patient whose goals have transitioned to comfort, consider the following physical, psychosocial-spiritual, and practical interventions

- **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 terminal secretions (death rattle):
    - ◊ Educate patient and caregiver
    - ◊ Reduce parenteral and enteral fluids
    - ◊ Reposition the patient
    - ◊ Provide gentle oropharyngeal suctioning (avoid deep suctioning)
    - ◊ Utilize non-pharmacologic interventions first before anti-secretory agents
  - ▶ Treat dyspnea by adjusting the dose of medication ([PAL-11](#))
  - ▶ Treat delirium ([PAL-24](#)) See [NCCN Guidelines for Distress Management](#)
  - ▶ Consider proportional sedation for refractory symptoms ([PAL-33](#))
  - ▶ Be prepared to discuss a request for organ donation and autopsy
- **Psychosocial-spiritual**
  - ▶ Educate the patient/family/caregiver about the signs and symptoms of dying and the rationale for discontinuation of treatments or medications that may not add to the patient's comfort
  - ▶ Consider consults to psychosocial-spiritual providers, including but not limited to social workers, chaplains, child life specialists, and psychologists 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. 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
  - ▶ Facilitate virtual family visits, if in-person visits are restricted or not possible
  - ▶ Provide information on funeral planning, if desired
  - ▶ Inform other involved health care professionals of patient's death

[After-Death Interventions \(PAL-34\)](#)

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### PROPORTIONAL SEDATION

- **Proportional sedation (formerly known as palliative sedation) is the intentional lowering of awareness towards, and including, unconsciousness for patients with severe and refractory symptoms with the primary goal of symptom relief.**
- **Refractory symptoms are symptoms that cannot be adequately managed despite comprehensive, interprofessional palliative care that does not compromise consciousness.**
- **Refer to institutional guidelines/policy for additional guidance.**
- **"A patient who is suffering from a terminal illness and who is experiencing great pain has no legal barriers to obtaining medication, from qualified physicians, to alleviate suffering, even to the point of unconsciousness and hastening death." -Justice O'Connor (see *Vacco v Quill* and *Washington v Glucksberg*, 1997).**
- **The NCCN Guidelines committee has replaced the term palliative sedation with proportional sedation. The change is intended to emphasize that the level of sedation should be proportionate to the patient's symptom burden.**

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DEATH	ASSESSMENT	AFTER-DEATH INTERVENTIONS
<p>Death →</p>	<p>A “peaceful death”:</p> <ul style="list-style-type: none"> <li>• Free from avoidable distress and suffering for the patient, family, and caregiver(s)</li> <li>• In general accord with the patient’s and family’s wishes</li> <li>• Consistent with clinical, cultural, spiritual, and ethical standards</li> </ul>	<p>For family and caregiver(s)</p> <ul style="list-style-type: none"> <li>• Immediate after-death care:                             <ul style="list-style-type: none"> <li>▸ Inform family (if not present) of death</li> <li>▸ Offer condolences</li> <li>▸ Provide the family time with the body</li> <li>▸ Involve chaplain to assess family’s desire for religious ritual or spiritual support</li> <li>▸ Remove tubes, drains, lines, and the foley catheter unless an autopsy is planned</li> <li>▸ Ensure culturally sensitive, respectful treatment of the body</li> <li>▸ Address survivor concerns about organ donation and/or autopsy</li> <li>▸ File the death certificate, complete forms, and provide necessary information for the funeral director and family as appropriate                                     <ul style="list-style-type: none"> <li>◊ Notify previous medical, palliative, and psychological care teams of patient’s death</li> </ul> </li> </ul> </li> <li>• Bereavement support:                             <ul style="list-style-type: none"> <li>▸ Formally express condolences on the patient’s death (eg, card, call, letter)</li> <li>▸ Refer to appropriate bereavement services within the institution or in the community</li> <li>▸ Facilitate a debriefing meeting with the family if they desire one</li> </ul> </li> <li>• Periodically assess and monitor family/caregiver for risk factors associated with complicated grief.</li> </ul> <p>For health care professionals</p> <ul style="list-style-type: none"> <li>• General support:                             <ul style="list-style-type: none"> <li>▸ Legitimize discussion of personal issues that impact patient care</li> <li>▸ Create a climate of safety for discussion of patient deaths</li> <li>▸ Provide regular opportunities for reflection and remembering for staff through a memorial ritual</li> </ul> </li> <li>• After-death support:                             <ul style="list-style-type: none"> <li>▸ Review medical issues related to the patient’s death                                     <ul style="list-style-type: none"> <li>◊ Explore concerns and questions regarding quality of patient care</li> </ul> </li> <li>▸ Review the family’s emotional responses to the patient’s death</li> <li>▸ Review the staff’s emotional responses to the patient’s death                                     <ul style="list-style-type: none"> <li>◊ Identify health care professionals at risk for complicated grief, moral distress, or compassion fatigue</li> <li>◊ Include nurses, nursing assistants, physician team members (including medical students, residents, and fellows), social workers, and chaplaincy, as appropriate</li> <li>◊ Consider a bereavement ritual for staff (eg, brief reading, moment of quiet)</li> </ul> </li> </ul> </li> </ul>

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**PALLIATIVE CARE DRUG APPENDIX**

Condition	Recommended Agents and Dosage by Estimated Life Expectancy and Symptom Etiology
<b>Pain</b>	<ul style="list-style-type: none"> <li>• Please see <a href="#">NCCN Guidelines for Adult Cancer Pain (PAIN-G)</a> for detailed information on opioid principles, prescribing, titration, maintenance, and safety. Be aware of state and local regulations regarding opioid prescriptions.</li> </ul>
<b>Dyspnea</b> ( <a href="#">PAL-11</a> )	<p><b>Life Expectancy: Years; Year to Months; and Months to Weeks</b></p> <ul style="list-style-type: none"> <li>• <b>General: Opioids<sup>a</sup></b> <ul style="list-style-type: none"> <li>▶ Opioids in low doses, with titration as appropriate, can be used to treat dyspnea that is resistant to other therapies.</li> <li>▶ Base dosing on patient's opioid requirement. If patient's opioid requirement is unknown, start with low doses and titrate up as appropriate.</li> </ul> </li> <li>• <b>Fluid overload: Furosemide, PRN dosing as per clinical situation</b></li> </ul>
<b>Dyspnea</b> ( <a href="#">PAL-12</a> )	<p><b>Life Expectancy: Weeks to Days (dying patient)</b></p> <ul style="list-style-type: none"> <li>• <b>Anxiety: Benzodiazepines (eg, lorazepam, 0.25–1 mg PO every 2–4 h PRN)</b></li> </ul>
<b>Secretions</b> ( <a href="#">PAL-12</a> )	<ul style="list-style-type: none"> <li>• <b>Excessive secretions: Glycopyrrolate, 0.2–0.4 mg IV or SC every 4 h PRN (less sedating), scopolamine, PRN/1.5-mg patches, 1–2 patches every 72 h OR atropine, 1% ophthalmic solution 1–2 drops SL every 2 h PRN (caution in asthma), OR hyoscyamine, 0.125–0.25 mg PO or SL every 4 h with max dose of 1.5 mg daily</b></li> </ul>
<b>Anorexia/ Cachexia<sup>1</sup></b> ( <a href="#">PAL-13</a> and <a href="#">PAL-14</a> )	<p><b>Life Expectancy: Years; Year to Months; Months to Weeks; Weeks to Days (dying patient)</b></p> <ul style="list-style-type: none"> <li>• <b>Counsel family and patients about risks (eg, thrombosis), benefits, and options for cachexia treatment (eg, stopping therapy if ineffective)</b></li> <li>• <b>Gastroparesis (early satiety): Metoclopramide 5–10 mg PO QID 30 min before meals and QHS Low/no appetite (avoid in setting of complete bowel obstruction): Megestrol acetate, PO<sup>2</sup> OR olanzapine, 2.5–5 mg/d PO OR dexamethasone 3–8 mg/d</b></li> <li>• <b>Clinicians may choose not to prescribe pharmacologic intervention for cancer cachexia treatment</b></li> </ul>

[Abbreviations Key \(PAL-A 5 of 5\)](#)

<sup>a</sup> Use caution if using opioids and benzodiazepines in combination outside of end-of-life care because of the risk of respiratory depression.

<sup>1</sup> Roeland EJ, Bohlke K, Baracos VE, et al. Management of cancer cachexia: ASCO guideline. J Clin Oncol 2020;38:2438-2453.

<sup>2</sup> Ruiz Garcia V, López-Briz E, Carbonell Sanchis R, et al. Megestrol acetate for treatment of anorexia-cachexia syndrome. Cochrane Database Syst Rev 2013;2013:CD004310.

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[Continued](#)**PAL-A**  
**1 OF 5**



### PALLIATIVE CARE DRUG APPENDIX

Condition	Recommended Agents and Dosage by Estimated Life Expectancy and Symptom Etiology
<b>Nausea and Vomiting (NV)- Initial Treatment (PAL-15)</b>	<p><b>Life Expectancy: Years; Year to Months; Months to Weeks; and Weeks to Days (dying patient)</b></p> <p><b>Common Etiologies</b></p> <ul style="list-style-type: none"> <li>• See <a href="#">NCCN Guidelines for Antiemesis</a> for chemotherapy/radiation-induced NV</li> <li>• <b>Gastroparesis:</b> Metoclopramide, 5–10 mg PO QID 30 min before meals and QHS (avoid in setting of complete bowel obstruction)</li> <li>• <b>CNS involvement:</b> Dexamethasone, 4–8 mg PO BID–TID</li> <li>• <b>Gastric outlet obstructions:</b> Dexamethasone, 4–8 mg/d PO; proton pump inhibitor</li> <li>• <b>Gastritis/GERD:</b> Proton pump inhibitor OR H2 blocker</li> <li>• <b>Medication-induced gastropathy:</b> Proton pump inhibitor OR metoclopramide, 5–10 mg PO QID 30 min before meals and QHS</li> </ul> <p><b>Nonspecific NV</b></p> <ul style="list-style-type: none"> <li>• <b>Dopamine receptor antagonists or 5-HT3 receptor antagonists</b> <ul style="list-style-type: none"> <li>▸ Olanzapine, 2.5–5 mg PO 1–2 times daily starting QHS</li> <li>▸ Haloperidol, 0.5 mg PO TID OR metoclopramide, 5–10 mg PO QID 30 min before meals and QHS OR prochlorperazine, 5–10 mg PO 3–4 times/d, maximum 40 mg/d OR ondansetron, 4 mg PO every 4 h or 8 mg PO every 8 h</li> </ul> </li> <li>• <b>Contributing anxiety:</b> Lorazepam, 0.5–1 mg PO every 4 h PRN</li> <li>• <b>Vertiginous component:</b> Anticholinergic AND/OR antihistamine</li> </ul>
<b>Nausea and Vomiting (NV)- Initial Treatment (PAL-16)</b>	<p><b>Life Expectancy: Years; Year to Months; Months to Weeks; and Weeks to Days (dying patient)</b></p> <ul style="list-style-type: none"> <li>• <b>Consider appropriate route of administration</b> <ul style="list-style-type: none"> <li>▸ 1) Prescribe PO, SL, or rectal agent and titrate to maximum benefit</li> <li>▸ 2) If NV persists, provide PRN, scheduled, or continuous parenteral infusion as necessary</li> <li>▸ 3) Consider SC administration as an alternative</li> </ul> </li> <li>• <b>Titrate to maximum benefit and tolerance:</b> olanzapine, prochlorperazine, haloperidol, or metoclopramide</li> <li>• <b>For continued NV, consider additional agents:</b> <ul style="list-style-type: none"> <li>▸ Dexamethasone, 4–8 mg/d PO; ondansetron, 4–8 mg PO every 6 h; scopolamine (patch or IV); meclizine, 25–100 mg/d PO; PO cannabinoid</li> </ul> </li> </ul>
<b>Constipation (PAL-17)</b>	<p><b>Life Expectancy: Years; Year to Months; Months to Weeks; and Weeks to Days (dying patient)</b></p> <ul style="list-style-type: none"> <li>• <b>Prophylaxis:</b> Start with an osmotic laxative if patient can tolerate the volume of liquid (polyethylene glycol BID) and add stimulant laxatives (senna BID or bisacodyl daily–TID) to achieve a goal of one non-forced bowel movement every 1–2 days</li> <li>• <b>Persistent constipation:</b> Bisacodyl suppository, one rectally daily–BID; polyethylene glycol, 17 gm/8 oz water PO BID; lactulose, 30 mL PO BID–QID OR 60 mL daily; sorbitol, 30 mL PO every 2 h x 3, then PRN; magnesium hydroxide, 30–60 mL PO daily–BID (avoid in renal failure); or magnesium citrate, 8 oz PO daily (avoid in renal failure)</li> <li>• <b>Resistant opioid-induced constipation:</b> <ul style="list-style-type: none"> <li>▸ If PO therapy is not effective, try enema</li> <li>▸ Consider methylnaltrexone, see prescribing information for weight-based dosing; naloxegol 12.5–25 mg daily PO; naldemedine 0.2 mg daily PO; lubiprostone 24 mcg BID PO; linaclotide 145–290 mcg daily PO</li> <li>▸ Not for postoperative ileus and mechanical bowel obstruction</li> </ul> </li> </ul>

[Abbreviations Key \(PAL-A 5 of 5\)](#)

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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.

[Continued](#)  
**PAL-A**  
**2 OF 5**

**PALLIATIVE CARE DRUG APPENDIX**

Condition	Recommended Agents and Dosage by Estimated Life Expectancy and Symptom Etiology
<b>Diarrhea (PAL-19)</b>	<p><b>Life Expectancy: Years; Year to Months; and Months to Weeks</b> If immunotherapy-induced diarrhea, see <a href="#">NCCN Guidelines for Management of Immunotherapy-Related Toxicities</a></p> <p><b>Grade 1 (mild)</b></p> <ul style="list-style-type: none"> <li>• General: Loperamide, 4 mg PO x 1 then 2 mg PO after each loose stool, up to 16 mg/d</li> <li>• Consider addition of bulk-forming agents with caution in patients on opioids</li> <li>• Diphenoxylate/atropine 1–2 tabs PO every 6 h PRN, maximum 8 tabs/d</li> </ul> <p><b>Grade 2 (moderate)</b></p> <ul style="list-style-type: none"> <li>• Initiate/continue loperamide, 4 mg PO x 1 then 2 mg PO after each loose stool, up to 16 mg/d</li> <li>• Diphenoxylate/atropine 1–2 tabs PO every 6 h PRN, maximum 8 tabs/d</li> <li>• Consider hyoscyamine, 0.125 mg PO/ODT/SL every 4 h PRN, max: 1.5 mg/d; atropine 0.5–1 mg SC/IM/IV/SL every 4–6 h PRN</li> <li>• C. diff-induced: see <a href="#">NCCN Guidelines for Prevention and Treatment of Cancer Related Infections (FEV-8)</a></li> <li>• Non-C. diff infection: Treat appropriately based on culture findings</li> </ul> <p><b>Grades 3/4 (severe, inpatient hospitalization w/ICU for Grade 4)</b></p> <ul style="list-style-type: none"> <li>• Initiate/continue loperamide, 4 mg PO x 1 then 2 mg PO after each loose stool, up to 16 mg/d</li> <li>• Diphenoxylate/atropine, 1–2 tabs PO every 6 h PRN, maximum 8 tabs/d</li> <li>• Consider hyoscyamine, 0.125 mg PO/ODT/SL every 4 h PRN, max: 1.5 mg/d; atropine 0.5–1 mg SC/IM/IV/SL every 4–6 h PRN</li> <li>• Consider octreotide, 100–200 mcg/d SC, every 8 h or by continuous infusion</li> </ul>
<b>Diarrhea (PAL-19)</b>	<p><b>Life Expectancy: Weeks to Days (dying patient)</b></p> <ul style="list-style-type: none"> <li>• Reevaluate ongoing antidiarrheal, anticholinergic agents</li> <li>• Consider tincture of opium</li> <li>• Atropine 0.5–1 mg SC/IV/SL every 4–6h PRN</li> <li>• Consider octreotide, 100–200 mcg SC every 8 h</li> <li>• Consider glycopyrrolate, 0.2–0.4 mg IV/SC every 4 h PRN</li> </ul>
<b>Malignant Bowel Obstruction (PAL-20)</b>	<p><b>Life Expectancy: Years; Year to Months; Months to Weeks; and Weeks to Days (dying patient)</b></p> <ul style="list-style-type: none"> <li>• Reduce opioid dose or rotate opioid</li> <li>• Metoclopramide, 5–10 mg PO QID 30 min before meals an QHS; avoid in the setting of complete obstruction</li> <li>• Dexamethasone, 4–12 mg IV daily, discontinue if no improvement in 3–5 days</li> <li>• Scopolamine (patch or IV); hyoscyamine, 0.125 mg PO/ODT/SL every 4 h PRN; glycopyrrolate, 0.2–0.4 mg IV every 4 h PRN</li> <li>• Octreotide, 100–300 mcg SC BID–TID or 10–40 mcg/h continuous SC/IV infusion; if prognosis &gt;8 weeks, consider long-acting release (LAR) or depot injection</li> </ul>

[Abbreviations Key \(PAL-A 5 of 5\)](#)**Note:** All recommendations are category 2A unless otherwise indicated.**Clinical Trials:** NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.[Continued](#)PAL-A  
3 OF 5



### PALLIATIVE CARE DRUG APPENDIX

Condition	Recommended Agents and Dosage by Estimated Life Expectancy and Symptom Etiology
<p><b>Sleep/Wake Disturbance</b> (<a href="#">PAL-22</a>)</p>	<p><b>Life Expectancy: Years; Year to Months; and Months to Weeks</b></p> <p><b>Isolated sleep-onset insomnia</b></p> <ul style="list-style-type: none"> <li>• Dual orexin receptor antagonist (DORA)                             <ul style="list-style-type: none"> <li>▸ Daridorexant, 25–50 mg PO 30 min before bedtime</li> <li>▸ Lemborexant, 5–10 mg PO QHS</li> <li>▸ Suvorexant, 10–20 mg PO QHS</li> </ul> </li> <li>• Ramelteon, 8 mg PO QHS</li> <li>• Melatonin, 1–5 mg PO QHS</li> <li>• Benzodiazepine receptor agonist (BZRA) (caution in patients who are older or frail)                             <ul style="list-style-type: none"> <li>▸ Zolpidem, 5-10 mg PO QHS for IR tablet, 6.25-12.5mg for ER tablet</li> <li>▸ Eszopiclone, 1–3 mg PO QHS</li> <li>▸ Zaleplon, 10–20 mg PO QHS</li> </ul> </li> </ul> <p><b>Sleep maintenance</b></p> <ul style="list-style-type: none"> <li>• DORA (see above)</li> <li>• Doxepin, 3–6 mg PO QHS (caution in patients who are older or frail)</li> </ul> <p><b>Additional agents for insomnia</b></p> <ul style="list-style-type: none"> <li>• Sedating antidepressants                             <ul style="list-style-type: none"> <li>▸ Mirtazapine, 7.5–30 mg PO QHS (better tolerated in patients who are older or frail)</li> <li>▸ Trazodone, 25–100 mg PO QHS</li> <li>▸ TCAs such as amitriptyline or nortriptyline (caution in patients who are older or frail)</li> </ul> </li> <li>• Sedating antipsychotics (monitor for extrapyramidal symptoms [EPS])                             <ul style="list-style-type: none"> <li>▸ Olanzapine, 2.5–5 mg PO QHS</li> <li>▸ Quetiapine, 12.5–25 mg PO QHS</li> </ul> </li> <li>• Benzodiazepines                             <ul style="list-style-type: none"> <li>▸ Lorazepam, 0.5–1 mg PO QHS (caution in patients who are older or frail)</li> </ul> </li> <li>• Medical cannabis                             <ul style="list-style-type: none"> <li>▸ Oral form preferred in 2:1 or 1:1 ratios (caution in patients who are older or frail)</li> </ul> </li> </ul> <p><b>Daytime sedation</b></p> <ul style="list-style-type: none"> <li>• Caffeine, 100–200 mg PO every 6 h, last dose 4 PM</li> <li>• Methylphenidate, 2.5–20 mg PO BID, second dose no later than 6 h before bedtime</li> <li>• Dextroamphetamine, 2.5–10 mg PO BID, second dose no later than 12 h before bedtime</li> <li>• Modafinil, 100–400 mg PO each morning</li> <li>• Dextroamphetamine and amphetamine: 10-60 mg per day in 1 to 3 divided dose</li> </ul> <p><b>Restless legs syndrome (RLS)<sup>b</sup></b></p> <ul style="list-style-type: none"> <li>• Dopamine agonists                             <ul style="list-style-type: none"> <li>▸ Intermittent                                     <ul style="list-style-type: none"> <li>◊ Carbidopa-levodopa, 25/100 mg PO QHS PRN</li> </ul> </li> <li>▸ Chronic                                     <ul style="list-style-type: none"> <li>◊ Ropinirole, 0.25 mg PO 1–3 h before bedtime</li> <li>◊ Pramipexole, starting dose 0.125 mg PO QHS, 2–3 h before bedtime, may require titration</li> </ul> </li> </ul> </li> <li>• Intermittent                             <ul style="list-style-type: none"> <li>▸ Clonazepam, 1–2 mg PO QHS PRN</li> </ul> </li> <li>• Chronic:                             <ul style="list-style-type: none"> <li>▸ Pregabalin, 50–450 mg 1-3 h before bedtime</li> <li>▸ Gabapentin, 100–2400 mg in divided doses 2 h prior to bedtime If divided dose: One-third of total daily dose given midday, remaining two-thirds of the total daily dose given in the evening</li> </ul> </li> </ul>

[Abbreviations Key and Footnotes](#)

([PAL-A 5 of 5](#))  
[Continued](#)

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**PALLIATIVE CARE DRUG APPENDIX**

Condition	Recommended Agents and Dosage by Estimated Life Expectancy and Symptom Etiology
<b>Sleep/Wake Disturbance</b> ( <a href="#">PAL-22</a> )	<b>Life expectancy: Weeks to Days (dying patient)</b> • Titrate dose of existing pharmacotherapy
<b>Delirium</b> ( <a href="#">PAL-23</a> )	<b>Life Expectancy: Years; Year to Months; and Months to Weeks</b> • Maximize nonpharmacologic approaches when possible <b>Mild/Moderate Delirium</b> • Haloperidol, 0.5–2 mg PO BID/TID • Alternatives: Risperidone, 0.5–2 mg PO BID; olanzapine, 5–20 mg PO daily; or quetiapine fumarate, 25–200 mg PO/SL BID <b>Severe Delirium (agitation)</b> • Haloperidol, 0.5–2 mg IV every 1–4 h PRN • Alternatives: Olanzapine, 2.5–7.5 mg PO/SL every 2–4 h PRN (maximum = 30 mg/d); chlorpromazine, 25–100 mg PO/PR/IV every 4 h PRN for-patients who are bedbound. For direct IV injection, administer diluted solution slow IV at a rate not to exceed 1 mg/minute. To reduce the risk of hypotension, patients receiving IV chlorpromazine must remain lying down during and for 30 minutes after the injection. • High-dose neuroleptic-refractory: Consider adding lorazepam, 0.5–2 mg SC/IV every 4 h
<b>Delirium</b> ( <a href="#">PAL-24</a> )	<b>Life Expectancy: Weeks to Days (dying patient)</b> • Upward titrate haloperidol, risperidone, and olanzapine High-dose neuroleptic-refractory: Upward titrate lorazepam • Consider rectal or IV haloperidol • Consider chlorpromazine, 25–50 mg PO/PR QHS with or without lorazepam, 0.5–2 mg SC/IV every 6 h
<b>Proportional Sedation</b> ( <a href="#">PAL-33</a> )	<b>Imminently dying patient</b> • Refer to institutional guidelines and policy • Midazolam or lorazepam, continuous infusion • Phenobarbital or pentobarbital • Propofol, continuous infusion

**Abbreviations Key**

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

<sup>b</sup> Avoid these agents (ie, ropinirole, pramipexole) when dopamine antagonists (eg, haloperidol, olanzapine, quetiapine) are being utilized.

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**ABBREVIATIONS**

<b>ADL</b>	<b>activities of daily living</b>	<b>LAR</b>	<b>long-acting release</b>
<b>AND</b>	<b>allow natural death</b>	<b>MAID</b>	<b>medical aid in dying</b>
<b>BiPAP</b>	<b>bilevel positive airway pressure</b>	<b>MOLST</b>	<b>Medical Orders for Life-Sustaining Treatment</b>
<b>BZRA</b>	<b>benzodiazepine receptor agonist</b>	<b>NV</b>	<b>nausea and vomiting</b>
<b>C. diff</b>	<b>Clostridioides difficile</b>	<b>PAMORA</b>	<b>peripherally acting mu-opioid receptor antagonist</b>
<b>CNS</b>	<b>central nervous system</b>	<b>POLST</b>	<b>Physician Orders for Life-Sustaining Treatment</b>
<b>CPAP</b>	<b>continuous positive airway pressure</b>	<b>PRN</b>	<b>as needed</b>
<b>CPR</b>	<b>cardiopulmonary resuscitation</b>	<b>SVC</b>	<b>superior vena cava</b>
<b>DNAR</b>	<b>do not attempt resuscitation</b>	<b>TCA</b>	<b>tricyclic antidepressant</b>
<b>DNR</b>	<b>do not resuscitate</b>	<b>TPN</b>	<b>total parenteral nutrition</b>
<b>DORA</b>	<b>dual orexin receptor antagonist</b>	<b>UTI</b>	<b>urinary tract infection</b>
<b>DSM</b>	<b>Diagnostic and Statistical Manual of Mental Disorders</b>		
<b>ECOG</b>	<b>Eastern Cooperative Oncology Group</b>		
<b>EPS</b>	<b>extrapyramidal symptoms</b>		
<b>GERD</b>	<b>gastroesophageal reflux disease</b>		
<b>GI</b>	<b>gastrointestinal</b>		
<b>G-tube</b>	<b>gastrostomy tube</b>		
<b>GVHD</b>	<b>graft-versus-host disease</b>		
<b>HIV</b>	<b>human immunodeficiency virus</b>		
<b>IBS</b>	<b>irritable bowel syndrome</b>		
<b>ICU</b>	<b>intensive care unit</b>		

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### NCCN Categories of Evidence and Consensus

<b>Category 1</b>	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
<b>Category 2A</b>	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
<b>Category 2B</b>	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
<b>Category 3</b>	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

All recommendations are category 2A unless otherwise indicated.

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# NCCN Guidelines Version 1.2024 Palliative Care

## Discussion

This discussion corresponds to the NCCN Guidelines for Palliative Care. Last updated: April 24, 2023.

## Table of Contents

Overview .....	2
Guidelines Update Methodology .....	2
Literature Search Criteria .....	2
Sensitive/Inclusive Language Usage .....	3
Palliative Care in Oncology .....	3
Impact of Palliative Care .....	4
Role of Hospice Care .....	5
Training in Palliative Care .....	6
Communication and Advance Care Planning in Palliative Care .....	7
Communication Skills Training .....	8
NCCN Guidelines for Palliative Care .....	9
Indications of Palliative Care Need .....	9
Comprehensive Assessment .....	9
Palliative Care Interventions .....	11
Anti-Cancer Therapy and Shared Decision-Making Considerations ..	12
Advance Care Planning .....	13
Symptom Management .....	14
Pain .....	15
Dyspnea .....	15
Anorexia/Cachexia .....	16

Nausea and Vomiting .....	18
Constipation .....	19
Diarrhea .....	20
Malignant Bowel Obstruction .....	21
Fatigue/Weakness/Asthenia .....	22
Sleep/Wake Disturbances Including Insomnia and Sedation .....	22
Delirium .....	23
Malignant Wounds .....	24
Psychosocial Distress – Social Support/Resource Management .....	24
Palliative Care Reassessment .....	25
End-of-Life Care Issues .....	26
Preparing Patients/Families/Caregivers for End of Life and Transition to Hospice Care .....	26
Requests for Hastened Death or Medical Aid in Dying .....	26
Shared Decision-Making in the Care of the Imminently Dying Hospitalized Patient .....	27
Palliative Sedation .....	28
A Peaceful Death .....	28
After-Death Care Interventions .....	29
Putting Palliative Care Guidelines into Practice .....	29
Psychosocial Support for Oncology and Palliative Care Providers .....	30
Conclusion .....	31
Table 1: Palliative Care Internet Resources for Clinicians .....	33
References .....	34





## 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, radiation 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 1.9 million people are expected to be diagnosed with cancer in the United States in 2023, and 609,820 people are expected to die of the disease.<sup>1</sup> Global cancer rates are increasing, with an associated rise in the number of cancer survivors living with symptoms and disabilities as a result of their disease and/or its treatment (see the [NCCN Guidelines for Survivorship](#)).<sup>2-4</sup> 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.<sup>5</sup> Integration of palliative care with disease-directed care may help to address the challenges faced by oncology patients and their families.

The Center to Advance Palliative Care (CAPC; [www.capc.org](http://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.”<sup>6</sup> During the past 20 years, increasing attention has been paid to quality-of-life issues in oncology throughout the disease trajectory.<sup>3,7-12</sup> 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.

## Guidelines Update Methodology

The complete details of the Development and Update of the NCCN Guidelines are available at [www.NCCN.org](http://www.NCCN.org).

## Literature Search Criteria

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 published since the previous Guidelines update, using the following search terms: (palliative care OR hospice OR end of life) AND (cancer OR 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, Phase II; Clinical Trial, Phase III; Clinical Trial, Phase IV; Guideline; Practice Guideline; Randomized Controlled Trial; Meta-Analysis; Systematic Reviews; and Validation Studies. The data from key PubMed articles as well as articles from additional sources deemed as relevant to these Guidelines as discussed by the panel during the Guidelines update have been included in this version of the Discussion section. Recommendations for which high-level evidence is lacking are based on the panel’s review of lower-level evidence and expert opinion.



## **Sensitive/Inclusive Language Usage**

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

## **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; promote adaptive coping; and 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; 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.<sup>13-17</sup> Palliative care becomes the main focus of care when disease-directed, life-prolonging therapies are no longer effective, appropriate, or desired.

Palliative care should be initiated by the primary oncology team, and should be augmented through collaboration with palliative care specialists in an interprofessional team (including but not limited to board-certified palliative care physicians, advanced practice providers, nurses, dietitians, social workers, mental health professionals, chaplains, and pharmacists) to address intractable symptoms and/or complex psychosocial issues.<sup>18</sup> Additionally, palliative care 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 when appropriate. 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 or other care facility. 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](http://www.aahpm.org)), National Hospice and Palliative Care Organization (NHPCO, [www.nhpc.org](http://www.nhpc.org)), and the CAPC ([www.capc.org](http://www.capc.org)) 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.<sup>16,17,19-32</sup>

**Impact of Palliative Care**

Studies have shown that the integration of palliative care into the cancer care continuum enhances cancer care resulting in improved patient outcomes across multiple measures, including quality of life, symptom intensity, and end-of-life care. In addition, patients with advanced cancer who receive palliative care concurrent with standard oncology care consistently experience equal or better overall survival.

**Survival**

Several groups have investigated the potential survival benefit associated with the provision of palliative care to patients with cancer. A remarkable study suggested that early introduction of palliative care does not only improve quality of life for patients with advanced cancer but can also improve survival.<sup>33</sup> 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.<sup>34</sup> Similarly, a retrospective analysis of 609 patients with terminal cancer suggested that increased duration of palliative care services was positively correlated with survival time.<sup>35</sup> In another study, home-based palliative care was associated with an equal or longer survival compared to inpatient palliative care in patients with cancer.<sup>36</sup>

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%,  $P = .038$ ).<sup>37</sup> 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.<sup>38</sup>

Further, 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.<sup>39</sup>

**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 specialized palliative care early, particularly those with advanced cancer ( $n = 1766/2454$ ), had the most pronounced effects on quality of life.<sup>40</sup> 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.<sup>41,42</sup> 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.<sup>43</sup>

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.<sup>44</sup> Compared with a care model in which palliative care was provided on an as-needed basis, standardized early palliative care also increased satisfaction with cancer care among caregivers of patients with advanced cancer.<sup>45</sup>

**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.<sup>46</sup> 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.<sup>47</sup> In one trial, patients receiving early palliative care were less likely to receive intravenous (IV) chemotherapy in the last 60 days of life (odds ratio [OR], 0.47; 95% CI, 0.23–0.99; *P* = .05),<sup>48</sup> likely because these patients had a more accurate understanding of their prognosis, which impacted decisions about their care.<sup>49</sup> 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.<sup>34</sup> 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.<sup>50</sup>

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.<sup>51–55</sup> 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.<sup>56</sup>

**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 8 weeks of diagnosis.<sup>57</sup> 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.<sup>58</sup>

In addition to improvement in quality of life and survival as discussed above, specialist palliative care has also been linked to cost savings. Earlier palliative care consultations have been associated with decreased health care costs for patients with advanced cancer, including those with multiple comorbidities.<sup>59–61</sup> According to recent data, dedicated palliative care units and programs can be cost-effective and favorably impact health system finances.<sup>62,63</sup>

**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 receive highly intensive end-of life care.<sup>64</sup> Furthermore, administration of cancer-directed treatments late in the course of cancer care, including in the last days of life, is growing more common,<sup>65,66</sup> and oncologists have reported that they have found hospice regulations and reimbursement limitations to be too restrictive.<sup>67</sup> Overall, provision of end-of-life care has been shown to be inconsistent and widely variable across regions, even among comprehensive cancer centers.<sup>64,68</sup>

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.<sup>69</sup> 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 who have been enrolled in hospice.<sup>70</sup> Additionally, analyses of data from 3069 deceased patients who had been >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.<sup>71</sup>

Unfortunately, many studies have suggested that palliative and hospice care often go underutilized.<sup>54,72-78</sup> 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 to up to 62% for prostate cancers.<sup>72</sup> Despite the 6-month prognosis eligibility, the median length of hospice service (LOS) for Medicare patients with cancer in 2016 was 19 days.<sup>79</sup> Approximately 28% of patients receiving hospice care died or were discharged within 7 days of admission to hospice care.<sup>79</sup> Thus, barriers to early referrals still exist.<sup>17,75</sup> 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.<sup>80</sup> By establishing hospice referrals as a quality improvement measure, one health system reported that median LOS in hospice doubled within a year of implementation.<sup>81</sup> 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.<sup>82</sup>

### **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](http://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](http://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](http://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.<sup>83</sup> 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.<sup>84</sup> In a survey study, oncology fellows reported that training on end-of-life issues and goal-of-care discussions mitigated burnout and distress.<sup>85</sup>

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 four regions of Japan.<sup>86</sup> 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, at the end of the Discussion section.

## **Communication and Advance Care Planning 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.<sup>87,88</sup> However, the report also found that few respondents had such discussions with their physicians.

Clinicians should assess and cultivate prognostic awareness and engage in advance care planning with patients and their families to ensure patient-centered care plans. Research suggests that the majority of patients queried express a desire to receive detailed prognostic information about their disease.<sup>89-92</sup> 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 patients who are middle-aged and older tend to be more optimistic and less accurate about their prognosis than their physicians; misunderstanding a disease progression timeline can impair timely decision-making, including discussions of preferences for cardiopulmonary resuscitation and other life-extending measures.<sup>93</sup>

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 spiritual care counselors, professional translators, the patient's personal clergy, and representatives from the patient's cultural community. Religious and cultural matters surrounding the beliefs and practices near the time of death should be anticipated and carefully managed.<sup>94-96</sup> 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.<sup>97</sup> 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.<sup>98</sup> 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.<sup>99</sup> Similar misconceptions also apply to palliative radiation therapy (RT). In a study of 384 patients with inoperable lung cancer, 64% of patients did not understand that their RT was not curative.<sup>100</sup> Notably, in a cohort of 686 patients with metastatic lung or colorectal cancer from CanCORS, only 16.5% were able to accurately state their prognosis.<sup>101</sup>

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.<sup>102-104</sup> 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.<sup>103,104</sup> Training in communication has been shown to improve clinician-patient communication<sup>105-109</sup> and to mitigate physician burnout and improve physician empathy and mood.<sup>110</sup> 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.<sup>111</sup> Additionally, the VOICE cluster randomized controlled trial recently demonstrated the effectiveness of patient-centered communication training for physicians caring for patients with advanced cancer.<sup>109</sup>

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 advance care planning and palliative care.<sup>112-116</sup> It is important to assess and cultivate prognostic awareness and patient goals and preferences in the context of clinical uncertainties or difficult news over the course of disease.<sup>117</sup> When patients accurately understand the goals of treatment, they are enabled to 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.<sup>118</sup> In addition, effective patient-physician communication has been shown to decrease patient stress, increase adherence to treatment, and improve outcomes.<sup>119,120</sup> Open communication with relatives or caregivers of patients with cancer is also critical, particularly when patients near the end of life.<sup>115,121</sup>



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.<sup>122</sup>

## **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 palliative care needs assessment, 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 NCCN Guidelines for Palliative Care have expanded the focus to all patients and family experiencing cancer throughout the disease trajectory, consistent with the Clinical Practice Guideline from ASCO.<sup>57</sup>

### **Indications of Palliative Care Need**

The primary oncology team should assess all patients at every visit for palliative care needs. Examples of palliative care needs or patients who may be at risk for higher palliative care needs include: 1) uncontrolled symptoms; 2) moderate to severe distress related to cancer diagnosis and/or therapy; 3) serious comorbid physical and/or psychiatric conditions; 4) complex psychosocial needs; 5) patient/family/caregiver concerns about the course of disease and decision-making; 6) patient/family/caregiver requests for palliative care; 7) spiritual/existential distress; 8) patient request for hastened death; 9) advanced cancers associated with high morbidity and mortality; 10) poor prognostic awareness; and/or 11) evidence of worsening prognosis. Elements of worsening prognosis may include a poor performance score (ECOG  $\geq 3$  or KPS  $\leq 50$ ), cachexia, persistent hypercalcemia, brain or cerebrospinal fluid

metastasis, persistent delirium, malignant bowel obstruction (MBO), superior vena cava syndrome, spinal cord compression, malignant effusions, or the need for palliative stenting or venting gastrostomy. Patients with identified needs and those who make a specific request for palliative care should undergo a full palliative care assessment. The Panel also recommends an assessment and integration of palliative care for patients with advanced cancers who receive hematopoietic cell transplant.<sup>123-125</sup>

Patients without an identified need should be re-evaluated 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 with palliative care needs should undergo a comprehensive palliative care assessment by their primary oncology team evaluating the benefits and burdens of anticancer therapy; decision-making capacity; coping strategies; personal goals/values/expectations; physical symptoms; functional status; psychosocial or spiritual distress (including financial toxicity); educational and informational needs; and cultural factors affecting care.<sup>7-9</sup> Patients with identified needs will likely benefit from palliative interventions. As part of a comprehensive assessment, oncology teams can consider whether consultation with specialty palliative care would be a beneficial addition to the care team, especially for patients with a poor prognosis or complex care needs.

### **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](http://www.NCCN.org)). Special attention should be given to the natural history of the specific tumor; the potential for response to further treatment (taking into consideration the patient's functional status); 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 Decision-Making Capacity, Coping Strategies, and Patient/Family/Caregiver Values, Goals, and Expectations***

Patients and their families should engage in advance care planning with their oncology team and be asked about their personal goals, values, expectations, and priorities. Assessing decision-making capacity and identifying appropriate surrogate decision-makers for patients who lack decision-making capacity (now or at some point in the future) is a key aspect of communication and decision-making. Further, understanding coping strategies and prognostic awareness is also central for communicating with patients with advanced cancer.<sup>126-130</sup> 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.<sup>116</sup>

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 and Functional Status***

Physical symptoms and changes in functional status can impact a patient's quality of life and how they tolerate cancer-directed therapy and even whether they are a candidate for anti-tumor therapy. The most common symptoms are pain, dyspnea, anorexia, cachexia, nausea, vomiting, constipation, diarrhea, MBO, fatigue, weakness, asthenia, insomnia, daytime sedation, delirium, lymphedema, and hormone-related symptoms.<sup>131</sup> Palliative interventions for symptoms are discussed individually in the *Symptom Management* section; for management of lymphedema and hormone-related symptoms, please see SLYMPH-1 and SHRS-1 in the [NCCN Guidelines for Survivorship](#).

#### ***Assessment of Psychosocial Distress***

Assessment of psychosocial distress should include both the patient and the caregivers, and should focus on illness-related distress and psychosocial, spiritual, or existential needs according to the [NCCN Guidelines for Distress Management](#). For management of spiritual or existential needs, consultation with a palliative care specialist and/or spiritual or psychosocial resources (eg, chaplains, clinical psychologists, community resources, social workers) may be considered. Concerns regarding social support and resources (eg, home, family, community, or financial toxicity including access barriers) must also be assessed. Recommendations for the management of psychosocial distress can be found below and in the [NCCN Guidelines for Distress Management](#). Other concerns that may increase distress include employment (or loss of employment) and social isolation (or loneliness); these issues should be assessed to ensure appropriate interventions can be provided, as feasible and desired. Barriers barring access to palliative care services should be discussed, and common concerns such as financial toxicity or



geographical issues (eg, limited or difficult transportation) should be addressed.

### ***Assessment of Educational and Informational Needs and Cultural Factors Affecting Care***

The values and preferences of patients and families regarding 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.<sup>95,132</sup>

### ***Criteria for Consultation with Palliative Care***

Palliative care consultation can be considered for all patients with advanced cancer, and especially for those with complex care needs based on patient characteristics, social circumstances, and/or anticipatory bereavement issues. The oncology team should consider consultation for patients with 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 level of psychological distress based on standardized distress screening (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. If applicable, concerns regarding a patient's decision-making capacity should also be assessed; for some approaches, see the [NCCN Guidelines for Older Adult Oncology](#).

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 use and/or concerns regarding substance use disorders, financial limitations, limited access to care, family discord, intensely dependent relationships, spiritual or existential distress, unresolved or multiple prior losses, dependent children and/or older relatives living in the household, care planning for children of a parent with poor prognosis, and/or support for active caregivers.

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 intra- or inter-team conflict, compassion fatigue, moral distress and/or ethical concerns, communication regarding complex decision-making, or burnout are present. For more information regarding psychosocial issues affecting care providers, see the section on *Psychosocial Support for Oncology and Palliative Care Providers*.

### **Palliative Care Interventions**

The oncology team should ensure anticancer therapy and appropriate treatment of comorbid physical and psychosocial conditions as medically indicated and concurrent with patient-centered care plans, including coordination of care with other health care providers. The oncology team should integrate palliative treatments following the specific recommendations described in these Guidelines. Referrals should be made as needed to mental health, social, and psychosocial support services; spiritual care; health care interpreters; or other specialists. The oncology team may be helpful in identifying additional support through religious organizations, schools, or other agencies in the community. Finally, the oncology team should promote adaptive coping, introduce advance care planning, participate in shared decision-making, collaborate with palliative care specialists and teams as needed (especially for



patients with complex care needs as indicated above), and ensure timely referral to hospice services when appropriate.

The Panel divided patients into three 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 a patient's prognosis is worsening include: decreased performance status (ECOG score  $\geq 3$ ; KPS score  $\leq 50$ ), 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.<sup>133-135</sup> Palliative care interventions for managing specific symptoms and the benefits and burdens of anticancer therapy are discussed below as outlined in the algorithm.

### **Anti-Cancer Therapy and Shared Decision-Making Considerations**

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.<sup>136-139</sup> Anticancer therapy may be conventional evidence-based treatment as outlined in the NCCN disease-specific Guidelines (available at [www.NCCN.org](http://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.<sup>140,141</sup> Palliative RT and/or interventional procedures also play an important role in the comprehensive care of patients with advanced cancer.<sup>142-148</sup> To assess the risk of serious complications in patients with neutropenic fever, the Panel recommends referring to the [NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections](#).

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.<sup>149,150</sup> 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 discuss the possibility of disease progression or recurrence. For an approach to decision-making in older adults and geriatric screening tools, see the [NCCN Guidelines for Older Adult Oncology](#).

Clinicians should provide primary palliative care to include both anticancer treatments aligned with patient goals and priorities and disease-related symptom management. The appropriateness of palliative RT or interventional procedures should be assessed, and palliative procedures conducted should be in line with the goals of care. 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 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 did not 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.<sup>151</sup> Studies have reported that, at times, anticancer therapy may continue beyond what is evidence-based for patients with advanced or metastatic disease.<sup>47,152,153</sup> In some cases, nonpharmacologic and/or integrative interventions (eg, cognitive-behavioral, massage, and music or art therapy) may be considered.

Patients with months to weeks to live should be provided with guidance regarding the anticipated course of the disease. Physicians should reassess prognostic awareness and goals of therapy. 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.<sup>150,151,154-156</sup> 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 refocusing care plan to achieve a better quality of life. It may be helpful to determine the patient and family’s prior experience(s) with end-of-life care. In addition, if appropriate, patients and families should be encouraged to complete any necessary legal documents. Clinicians, if appropriate, may assess and document the preferred location of death. Education and support related to care at the end of life should be offered.

In general, patients with weeks to days to live (eg, dying patients) and comfort-oriented goals 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. Referral for hospice care should be placed, if not already done. Culturally/spiritually significant rituals/ceremonies important at the end of life may be considered upon patient request.

### **Advance Care Planning**

The oncology team should assess and cultivate prognostic awareness, integrate discussions of personal values and preferences for current and future care while patients have a life expectancy of years to months. The patient’s decision-making capacity should also be assessed, and a surrogate decision-maker identified. Several 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.<sup>157-159</sup> Earlier integration of advance care planning discussions have been associated with less aggressive care and increased use of hospice,<sup>160,161</sup> while less aggressive care has been associated with an improved quality of life.<sup>162</sup> Studies suggest that most patients with cancer would prefer to die at home,<sup>163,164</sup> 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.<sup>165</sup> 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.<sup>166</sup> 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.<sup>167</sup>

Advance care planning should identify personal values, goals, expectations, and priorities and assess their congruence with those of the family/caregiver/health care team. Formal documents including advance directives, living wills, medical powers of attorney, and health care proxy should be completed. Any other documents delineating specific limitations regarding life-sustaining treatments (eg, cardiopulmonary resuscitation, mechanical ventilation, and artificial nutrition/hydration), as well as an open discussion about palliative care options such as hospice should be completed as appropriate. A 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.<sup>168</sup>

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.

Clinicians, if appropriate, may assess and document the preferred location of death. Most patients with cancer would prefer to spend one's remaining time at home,<sup>163,164</sup> 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.<sup>164,169</sup> 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.<sup>170</sup> Providing palliative care services has been shown to decrease deaths in ICUs.<sup>169</sup> A 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.<sup>164</sup> 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.<sup>171</sup> 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 weeks to days, the patient's decision regarding cardiopulmonary resuscitation and other life-sustaining treatments should be clarified and confirmed. Education about the benefits and limitations of CPR should be provided, and documentation of the resuscitation orders including in POLST/MOLST as per patient/family/caregiver preferences should be completed as appropriate. 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 complies with the patient's advance care plan. Education and support related to care at the end of life should be offered.

## Symptom Management

With regard to symptoms, the management of pain, dyspnea, anorexia/cachexia, nausea and vomiting, constipation, diarrhea, MBO, fatigue, delirium, and psychological distress are fundamental<sup>172-174</sup> and are discussed in detail below. Symptoms should be comprehensively assessed in all patients. In non-communicative patients, symptom intensity may be assessed using physical signs. Education should be provided to the patient/family/caregiver on the patient's condition and the risk/benefit of treatment options. In addition to education, psychosocial and emotional



support for the patient/family/caregiver(s) is also an important part of symptom management. 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, including opioid principles, prescribing, titration, maintenance, and safety. Clinicians should be aware of state and local regulations regarding opioid prescriptions.

It is also important to provide education on the role of pain medications and optimize psychosocial support for the patient/family/caregiver, customizing the education and support to the patient's particular situation. In addition, note additional considerations for dying patients in their last weeks of life. For example, nonpharmacologic and/or integrative interventions (eg, massage, art, or music therapy; acupuncture; relaxation; mindfulness; guided imagery) can be considered. Further, if feasible and desired, pain management should be balanced against reduced level of consciousness. If the patient's goals are comfort-oriented, avoid opioid dose reduction solely for decreased blood pressure or respiration rate. Routes of pain medication delivery may need to be modified as a patient approaches the end of life applying equianalgesic dose conversions. It is also important to recognize and treat opioid-induced neurotoxicity, including myoclonus and hyperalgesia. Single-fraction palliative RT may be used to address pain associated with bone metastases.<sup>147,148,175,176</sup> Study data suggest 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.<sup>176</sup>

### Dyspnea

Dyspnea is one of the most common symptoms in patients with advanced lung cancer.<sup>177</sup> 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.”<sup>178</sup> Potentially reversible underlying causes or comorbid conditions should be treated using chemotherapy or RT; therapeutic procedures for cardiac, pleural, or abdominal fluid<sup>179-181</sup>; bronchoscopic therapy; or bronchodilators, diuretics, steroids, antibiotics, transfusions, or anticoagulants for pulmonary emboli. Oxygen therapy for symptomatic hypoxia is also recommended.

Both pharmacologic and non-pharmacologic interventions have been investigated in the management of dyspnea. While there are little definitive data evaluating the effectiveness of dyspnea interventions,<sup>182,183</sup> the Panel members agree that there are sufficient data to make treatment recommendations.<sup>180,184</sup>

The Panel recommends first considering non-pharmacologic interventions including the use of handheld fans directed at the face,<sup>185,186</sup> cooler temperatures, stress management, relaxation therapy, and physical comfort measures. 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 after brief assessment of the effect of oxygen therapy on the individual patient.<sup>187</sup> If nonpharmacologic measures do not provide desired relief, pharmacologic interventions may be considered including opioids with or without benzodiazepines.<sup>180,182,183,188-191</sup>

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.<sup>182,192</sup> If fluid overload is thought to be a contributing factor for dyspnea, consider decreasing fluids and/or the addition of furosemide, based on the clinical situation.

Opioids, in low doses, with titration as appropriate, can be used to treat dyspnea that is resistant to other therapies. Morphine has undergone the most extensive investigation for treating dyspnea in patients with cancer and can be initiated in the opioid-naïve patient.<sup>193-198</sup> For patients receiving chronic opioids, the Panel recommends consideration of a 25% dose increase to treat symptomatic dyspnea. Opioid tolerance should be taken into consideration with dosing. Morphine should be avoided in patients with known renal compromise. For additional information on opioid medications and opioid titration, please see the [NCCN Guidelines for Adult Cancer Pain](#).

Scopolamine, atropine, hyoscyamine, and glycopyrrolate are options to reduce excessive secretions associated with dyspnea.<sup>199-203</sup> 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 still produce anticholinergic side effects.<sup>204-206</sup> Scopolamine can be administered subcutaneously or transdermally. Physicians should be aware that the onset of benefit for transdermal scopolamine patches is about 12 hours;<sup>207</sup> thus, they 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.

High-flow nasal oxygen and noninvasive mechanical ventilation are generally not available outside of the acute care 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.<sup>208</sup> 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.<sup>209</sup> Palliative RT can be considered for patients with symptomatic SVC syndrome or those who have respiratory obstruction by tumor mass.<sup>142,210</sup>

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. Options such as a time-limited trial of mechanical ventilation or therapy with high-flow nasal cannula may be considered, if consistent with the patient's goals and values. However, as life expectancy decreases, the role of mechanical ventilation and oxygen diminishes, and the role of other non-pharmacologic therapies and pharmacologic interventions increases. The Panel recommends first considering nonpharmacologic therapies, including educational, psychosocial, and emotional supportive measures. Other interventions to maintain cooler temperatures (including fans) should be considered. If nonpharmacologic measures do not provide desired relief, pharmacologic therapies may be considered, including: oxygen supplementation (if hypoxic and/or subjective relief is reported); opioids; and/or benzodiazepines. If fluid overload is a contributing factor, enteral and parenteral fluids should be decreased or discontinued; low-dose diuretics (such as furosemide) given PRN and dosed as per clinical scenario 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.<sup>211,212</sup> Many patients with cancer lose the desire to eat (anorexia), which contributes to cachexia. Cachexia can also occur independently from anorexia, as



proinflammatory cytokines and tumor-derived factors directly lead to muscle proteolysis.<sup>211,212</sup> Cachexia leads to asthenia (weakness), hypoalbuminemia, emaciation, immune system impairment, metabolic dysfunction, and autonomic failure. Cancer-related cachexia has also been associated with disease progression despite anti-cancer treatment, increased treatment toxicity, delayed treatment initiation, early treatment termination, shorter survival, and psychosocial distress.<sup>211-213</sup> A 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.<sup>214</sup>

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 dysgeusia, xerostomia, dental/jaw issues, intractable hiccups, mucositis, oropharyngeal candidiasis, depression, early satiety, nausea and vomiting, pain, fatigue, and pancreatic exocrine enzyme insufficiency, among others, and psychiatric evaluation may be considered if the patient has a history of an eating disorder or phobia/anxiety related to swallowing/eating challenges. Treatment may include modifying medications or 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.<sup>180,184,215</sup> A swallowing evaluation may also be considered. It is important to assess social and economic factors that may be contributing.

Appetite stimulants may be helpful (eg, megestrol acetate, dexamethasone, olanzapine) if increased appetite is an important aspect of quality of life.<sup>216-220</sup> Systematic reviews and meta-analyses of megestrol acetate demonstrate improved appetite and slight improvements in weight gain when using this drug to treat anorexia/cachexia in patients with

cancer.<sup>217,221</sup> 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.<sup>217</sup>

Some studies suggest that combination therapy approach with megestrol acetate and other therapies may yield improved outcomes for patients with cancer cachexia.<sup>221</sup> 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.<sup>222</sup> 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.<sup>223</sup>

The Panel noted that the quality of evidence for the routine use of megestrol acetate in patients with cancer cachexia is lacking, and clinicians must assess if the benefits of using megestrol acetate outweigh the risks. Clinicians should counsel patients about the risks (eg, thrombosis, death), benefits, and options for cachexia treatment (eg, stopping therapy if ineffective).

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.<sup>224</sup> 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.<sup>225</sup> 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.<sup>226</sup> 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 patients who are older 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,<sup>227</sup> consultation with a registered dietitian should be considered, because calorie-dense, high-protein supplementation has demonstrated some efficacy for weight stabilization.<sup>180,211,228-230</sup> 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.<sup>231</sup> 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.<sup>232</sup>

The goals and intensity of nutritional support change as life expectancy is reduced to weeks to days. Absence of hunger and thirst is normal in the dying patient, and nutritional support may not reverse weight loss in patients with advanced cancer. Education and emotional support should be provided regarding the natural history of the disease, as artificial nutrition and hydration may increase the risk of fluid overload, aspiration, infection, and hastened death. Overly aggressive enteral or parenteral nutrition therapies can actually increase the suffering of dying patients, and therefore, discontinuing previously initiated enteral or parenteral

nutrition near the end of life is appropriate, is ethically permissible, and may improve some symptoms.<sup>232-235</sup> 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.<sup>236</sup> 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.<sup>237</sup> Nausea and vomiting induced by chemotherapy or RT should be managed as outlined in the [NCCN Guidelines for Antiemesis](#). For patients who are looking for alternative treatment options for nausea and vomiting related to chemotherapy or RT may consider acupuncture.<sup>238</sup> Patients can also experience nausea and vomiting unrelated to chemotherapy and radiation, resulting from gastric outlet obstruction, bowel obstruction, constipation, opioid use, or hypercalcemia.<sup>239</sup> These causes should be identified and treated. Palliative RT should be considered for nausea and vomiting related to brain metastases.<sup>142,240,241</sup> 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 gastrostomy tube (G-tube). Many medications (including non-prescribed supplements and herbs) can also cause nausea and vomiting. Blood levels should be checked for possible culprits, such as digoxin, phenytoin, carbamazepine, and tricyclic antidepressants.<sup>242,243</sup> 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-HT<sub>3</sub> (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.<sup>244,245</sup> 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.<sup>245</sup> For anxiety-related nausea, the addition of benzodiazepines can be considered. If a vertiginous component to 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.<sup>246-248</sup> When patients experience dehydration, uremia, or hypercalcemia, the Panel recommends management with hydration and optimization of electrolytes.

For persistent nausea and vomiting, the Panel recommends titrating dopamine receptor antagonists to maximum benefit and tolerance.<sup>249-253</sup> In the setting of continued nausea and vomiting, consider additional drug classes with potential antiemetic properties: corticosteroids,<sup>254-256</sup> 5-HT<sub>3</sub> receptor antagonists,<sup>257-259</sup> anticholinergic agents and/or antihistamines,<sup>255</sup> or oral cannabinoids.<sup>260,261</sup> 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 patients taking opioid medications. For persistent/refractory nausea and vomiting, parenteral infusions can be provided 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 IV 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 are not successful.

### Constipation

Constipation occurs in approximately 60% of patients with advanced cancer and most patients treated with opioids.<sup>262,263</sup> Although several drugs including antacids, anticholinergic drugs (antidepressants, antispasmodics, phenothiazines, and haloperidol), and antiemetics are known to cause constipation,<sup>264</sup> 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.<sup>265</sup> Opioid-induced constipation (OIC) should be anticipated and treated prophylactically with a stimulant laxative with or without osmotic laxative.<sup>266</sup> 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,<sup>267</sup> 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.<sup>268</sup> 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.<sup>267</sup> Magnesium-containing products should be avoided in patients with renal failure. If gastroparesis is suspected, the addition of a prokinetic agent, such as metoclopramide, may be considered.

Peripherally acting  $\mu$ -opioid receptor antagonists may help to relieve resistant OIC while maintaining pain management.<sup>269</sup> Recent studies have shown that methylnaltrexone provided effective relief of OIC while preserving opioid-mediated analgesia.<sup>270,271</sup> Naloxegol, a similar peripherally acting  $\mu$ -opioid receptor antagonist, has also been studied for treating OIC in patients receiving chronic opioids for noncancer pain.<sup>272,273</sup> Based on these results, the Panel recommends considering use of methylnaltrexone every other day (no more than once a day) for patients experiencing OIC that has not responded to at least two different classes of 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  $\mu$ -opioid receptor antagonists such as methylnaltrexone.

Several other 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.<sup>274,275</sup> 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  $\mu$ -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 (IBS) and chronic idiopathic constipation.<sup>276,277</sup> The American Gastroenterological Association includes lubiprostone and linaclotide as recommended options for treating constipation associated with irritable bowel disorder.<sup>278</sup>

### 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.<sup>279</sup> 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).<sup>280-283</sup> Abdominal and pelvic RT (alone or as part of chemoradiation regimens) can also induce gastrointestinal toxicity resulting in diarrhea.<sup>281,282</sup>

The National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) are typically used for measuring diarrhea in this patient population.<sup>279</sup> 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, loperamide). If 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 Toxicities](#)).

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 diarrhea due to IBS, utilize cognitive behavioral interventions complementary to medication intervention.<sup>284</sup>

For patients with weeks to days of estimated life expectancy, the above interventions can be considered if consistent with the patient's 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 may be started on around-the-clock opioids or receive an increased dose of ongoing opioid regimens if appropriate.

### **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, considering prognosis and relative invasiveness of the intervention proposed.

For patients with years to months to live, surgery (eg, resection, bypass, diverting ostomy) 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.<sup>285</sup> 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 treatment 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.<sup>286</sup> 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 MBO 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.<sup>287-291</sup> 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.<sup>292,293</sup> Despite positive findings from several smaller randomized trials, a recent phase III trial of octreotide in 86 patients with MBO did not demonstrate a significant effect of this drug on days free of vomiting, number of vomiting episodes, symptom management, and other



secondary endpoints.<sup>294</sup> Note that if steroids are used, discontinue them if ineffective after 3 to 5 days.

A venting G-tube (inserted by interventional radiology, endoscopy, or surgery) or an endoscopically placed stent can also palliate symptoms of MBO.<sup>295-299</sup> 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.<sup>133,134</sup>

### **Fatigue/Weakness/Asthenia**

The data on methylphenidate for treating cancer-related fatigue have been mixed.<sup>300</sup> While some trials have suggested a dose-dependent benefit of this agent on fatigue symptoms,<sup>301,302</sup> other studies have not produced positive results.<sup>303</sup> Phase III randomized trials of modafinil for treating cancer-related fatigue suggested that modafinil had modest efficacy and was most effective for those with severe fatigue.<sup>304,305</sup> A Cochrane Database review summarized the existing data on psychosocial interventions for fatigue during palliative care for cancer.<sup>306</sup> 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.<sup>307-309</sup> In a 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.<sup>310</sup> Clinicians should assess the patient's desire to have insomnia and sedation treated.

The type and severity of sleep/wake disturbance should first be evaluated, including daytime impairments and co-sleeper observations. Primary sleep disorders, such as obstructive sleep apnea (OSA), restless legs syndrome, and periodic limb movement disorder, should be treated with

nocturnal continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP).<sup>311</sup> Restless legs syndrome, if present, can be treated with ropinirole, pramipexole with pregabalin, or carbidopa-levodopa.<sup>312-320</sup> Dopamine agonists (eg, ropinirole and pramipexole) should be avoided with concurrent usage of dopamine antagonists (eg, haloperidol, olanzapine, quetiapine). Worries and anxiety regarding cancer-related stressors 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.<sup>184,321-325</sup> Participation in a sleep study may be considered, if prognosis allows. A consult to a psychiatrist for a tailored exercise therapy program is also an appropriate intervention.

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; melatonin or the melatonin-receptor agonist ramelteon; and sedating antidepressants such as trazodone and mirtazapine.<sup>326</sup> The Panel suggests that mirtazapine may be especially effective in patients with concurrent depression and anorexia. Benzodiazepines should be avoided in patients who are older and those with cognitive impairment, because these agents have been shown to cause decreased cognitive performance.<sup>327</sup> Caution should be exercised when administering zolpidem due to the known risk of next-morning impairment.

For refractory daytime sedation, the Guidelines suggest several options. The central nervous system stimulants methylphenidate or dextroamphetamine should be given. 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 PRN.<sup>328</sup> 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.<sup>329</sup> The Panel also recommends caffeine as an additional option for refractory daytime sedation. The last dose of caffeine should be given no later than 4:00 PM. 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, Fifth Edition (DSM-5) criteria.<sup>330</sup> Potentially reversible causes should be identified and treated appropriately.<sup>331</sup> Delirium may present as either a hypoactive or a hyperactive subtype.<sup>332</sup> Recent studies have suggested that hypoactive delirium was the most prevalent subtype in patients receiving palliative care and that this condition is often underdiagnosed due to its presentation.<sup>333,334</sup> Delirium-inducing medications (eg, steroids, anticholinergics, benzodiazepines) should be reduced or eliminated as much as possible.<sup>335</sup> Non-pharmacologic interventions (eg, optimize sleep-wake cycle, address sensory impairment, provide glasses/hearing aids) 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.<sup>336,337</sup> 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.<sup>338-340</sup> 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.<sup>341,342</sup> Additionally, in one trial, the cohort receiving placebo with supportive care had longer overall survival times than the cohort receiving haloperidol.<sup>341</sup> Based on the mixed evidence available, the Panel recommends maximizing nonpharmacologic interventions prior to considering antipsychotic medications, if symptoms persist.

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.<sup>343</sup> 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.<sup>344-346</sup>

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, urinary tract infection (UTI), 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.<sup>347</sup> 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.

### **Malignant Wounds**

Malignant wounds are the result of cancerous cells infiltrating the skin and its supporting blood and lymph vessels, causing loss in vascularity that leads to tissue death. Malignant wounds may originate as a primary cancer or as a metastasis to the skin from a local or distant tumor.<sup>348</sup>

Malignant wounds may cause many distressing symptoms that negatively impact quality of life. In most cases, a combination of discharge, odor, bleeding, pruritis, local inflammation, and/or pain accompany the wound, requiring medical attention and treatment.<sup>349</sup>

The Panel recommends treating malignant wounds if potentially reversible in patients with an estimated life expectancy of years to months.

Treatment options include surgical debridement, skin grafting, wound-directed treatment with radiation/chemotherapy/hormonal therapy, vacuum-assisted wound closure, wound cleansing/irrigation, dressing changes, treating infection, optimizing nutrition/mobilization, and preventing wound spread.

In the dying patient, the Panel recommends interventions focused on symptom relief. For odor, wound cleansing/debridement, topical antibiotic gel, activated charcoal/silver sulfadiazine dressings, external odor absorbers, and/or avoiding strong “cover” odors are recommended. For infection, topical/systemic antibiotics and/or irradiated honey applications are recommended. For exudate, absorbent alginate, foam dressings, and/or drainage stoma appliance (if high volume) are recommended. For bleeding, hemostatic dressings (alginate, collagen, non-adherent gauze, gelfoam, sucralfate paste), oral antifibrinolytics, radiotherapy or embolization (if brisk bleeding), dark-colored linens, anxiolytics, and/or pain management are recommended. For pain, use of non-absorbent dressing or reducing frequency of dressing changes may be considered. Topical opioid and/or local anesthetic may be applied. Pain should be treated according to the [NCCN Guidelines for Adult Cancer Pain](#). For pruritis, topical doxepin cream, cooled hydrogel sheet dressings, and/or transcutaneous electrical nerve stimulation (TENS) trial are recommended. For body image, recommended strategies include maintaining symmetry in dressings, managing wound odor and exudate, and/or screening for depression or anxiety.

### **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.<sup>28,125,350,351</sup> A systematic review of patients with advanced cancer identified psychosocial resources among the factors that promoted personal growth during the experience of cancer.<sup>352</sup>



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, art and music therapy (if available), support groups, and physical medicine/rehabilitation training for transfers and repositioning.<sup>353-355</sup> Personal, spiritual, or cultural issues related to the patient's illness and prognosis should be addressed.<sup>356</sup> Bereavement risk and risk for persistent complex bereavement disorder should be assessed. Respite care for families and caregivers in crisis should be considered.

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. Child life services should be provided if appropriate and available, and clinicians should respond to caregiver-specific demands, stresses, and conflicts (consider social work referral). Medical interpreters/translators who are not related to the patient and family may be obtained as needed. Risk for persistent complex bereavement disorder should be reassessed. Culturally and spiritually congruent care should be ensured. Eligibility, readiness, and need for specialized palliative/hospice care including open access hospice programs (if available) 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 those for disease-specific NCCN Guidelines. The Panel reviewed end-of-life care outcomes from several surveys of North American citizens.<sup>357-360</sup> 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 Panel also recommends promoting adaptive coping strategies.<sup>126</sup> The oncology team should also consult specialized palliative care services, hospice, or an ethics committee when needed. Consultation with a mental health professional and/or addiction specialist to evaluate and treat undiagnosed psychiatric disorders and substance use disorders should be considered as appropriate. If psychosocial distress persists, palliative care options should be intensified, and patients should receive care 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.<sup>361</sup> Specialty 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 as appropriate. 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. Other involved health care professionals should be informed of the patient's death.

### Requests for Hastened Death or Medical Aid in Dying

The most appropriate initial response to a request for hastened death or medical aid in dying (MAID) is to explore the meanings behind that request and intensify palliative care interventions.<sup>362</sup> 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.<sup>363,364</sup> 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.<sup>362,365</sup> 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 MAID, under specified conditions, is legal in California,



Colorado, Hawaii, Maine, Montana, New Jersey, Oregon, Vermont, Washington, and Washington, D.C, euthanasia is not legal in any of the United States.<sup>362,366-371</sup> It is important for physicians to know the local legal status of MAID, as other states have pending legislation regarding either prohibiting or permitting MAID.<sup>362</sup> Several organizations have released position statements and/or helpful websites on the issue of MAID (see Table 1 at the end of the Discussion section).

### **Shared Decision-Making in the 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.<sup>372</sup> Caring for an imminently dying patient is intense for the patient, family, caregiver(s), and health care team. An international qualitative study described many of the common non-pharmacologic palliative care activities provided in the last days of life.<sup>373</sup> An end-of-life care order set for patients wishing to focus on comfort 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.

For patients whose goals shift to comfort at the end of life, the physical aspects of care for an imminently dying patient focus on adequate symptom management. 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.<sup>203,374,375</sup> 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 whose goals have transitioned to comfort focus on 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 patient/family/caregiver should be educated about the rationale for discontinuation of treatment or medications that may not add to the patient's comfort. The care plan may also include consultation with psychosocial providers, including but not limited to social workers, chaplains, child life specialists, and psychologists to meet the social and spiritual needs of the patient and their family/caregivers; 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 when possible; and enabling family presence around the clock as appropriate. If not already done, patient/family/caregiver wishes for resuscitation should be discussed and documented. In this context, 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 "Allow 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. If in-person visits are restricted or not possible, facilitate virtual visits.

**Palliative Sedation**

Palliative sedation is the intentional lowering of awareness towards, and including, unconsciousness for patients with severe and refractory symptoms. 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, especially for existential suffering.<sup>376,377</sup> Many providers do not support palliative sedation for patients not likely to die within 2 weeks, because at that point the absence of food or hydration could become the immediate physiologic cause of death. The Panel recommends referring to institutional guidelines/policy for additional guidance.

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,<sup>378-383</sup> which provides guidance for 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.<sup>384,385</sup> 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.<sup>386</sup> Prior to initiating palliative sedation, an ethics consult should be considered in accordance with institutional guidelines and state/national regulations.<sup>377</sup>

Palliative sedation is best performed by palliative care experts.<sup>387</sup> The most common sedatives used for palliative sedation are midazolam, lorazepam, propofol, phenobarbital, and pentobarbital by parenteral infusions.<sup>381</sup> Some studies have suggested that palliative sedation may also be feasible in the home setting and could be utilized in patients who wish to die at home.<sup>388,389</sup>

**A Peaceful Death**

These NCCN Guidelines 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.<sup>390-393</sup> 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.<sup>393</sup> End-of-life care should be flexible enough to ensure that the death is viewed as a peaceful death by those involved.<sup>393</sup> 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.”<sup>394</sup>

Final results of the prospective, longitudinal cohort Coping With Cancer study of 396 patients with advanced cancer and their caregivers 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.<sup>162</sup>

### **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 the family time with the body. Chaplain or other spiritual leader involvement to assess the 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 previous medical, palliative, and psychological care teams 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 persistent complex bereavement should be identified and offered support and treatment. Persistent complex bereavement disorder is a condition characterized by intense, prolonged symptoms of grief, coupled with functional impairment beyond 6 months post-loss.<sup>395-398</sup> Children of patients with cancer represent a uniquely at-risk population for psychosocial dysfunction. Additionally, a 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.<sup>399</sup>

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, Ovarian, and Pancreatic](#) and [NCCN Guidelines for 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.<sup>19-27,400</sup>

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 their expertise. Finally, the quality of palliative care should be monitored by institutional quality improvement programs.

The experiences of patients with cancer begin with 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.<sup>401,402</sup> This may be a sign of imperfect understanding of the disease and should be addressed directly and compassionately.<sup>402</sup> 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 assess and cultivate prognostic awareness and create a care plan that is consistent with the patient's 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, intra-team conflicts or disagreements, compassion fatigue, and ethical concerns or moral distress.<sup>403-407</sup> These syndromes can manifest as symptoms of depression, anxiety, fatigue, and low mental quality of life.<sup>408</sup> 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,<sup>403</sup> Shanafelt and Dyrbye,<sup>408</sup> and Sherman and colleagues.<sup>409</sup>



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 (eg, 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.<sup>410</sup> 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.<sup>411</sup> 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.<sup>411,412</sup> 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.<sup>413-415</sup> 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).<sup>416</sup>

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.<sup>403,417</sup> 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.<sup>417</sup>

Generally, evidence-based interventions for compassion fatigue, moral distress, and burnout in physicians are lacking. When asked to provide useful preventive measures and coping strategies, palliative care specialists recommended emphasizing the rewarding aspects of their work and strategies for “enhanced meaning-making.”<sup>418</sup> 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.<sup>419</sup> To this end, self-care was established as a core competency area for fellows in hospice and palliative medicine.<sup>419</sup> Examples and evidence for additional preventive strategies and solutions for oncologist burnout have been reviewed by Shanafelt and Dyrbye.<sup>408</sup>

## 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.<sup>93</sup> Using a decision aid, Smith et al found that most patients want honest information, even if it is bad news.<sup>420</sup> 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.<sup>421</sup> Providing information in a collaborative manner protects the autonomy of patients to make informed decisions based on potential treatment outcomes.<sup>422</sup> 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.<sup>101,420,423</sup> Even when cure is no longer possible, hope remains: hope



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# NCCN Guidelines Version 1.2024 Palliative Care

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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<sup>a</sup>**

<sup>a</sup>Adapted with permission from Khatcheressian J, Cassel JB, Lyckholm L, et al. Improving palliative and supportive care in cancer patients. *Oncology (Williston Park)*. 2005;19:1365-1376.

<b>Palliative Care Clinical Competencies</b>	
<a href="http://www.epec.net">www.epec.net</a>	Education in Palliative and End-of-Life Care (EPEC): Comprehensive curriculum covering fundamentals of palliative medicine; teaching guides
<a href="http://www.StopPain.org">www.StopPain.org</a>	Department of Pain Medicine and Palliative Care at Beth Israel Medical Center: Online education for physicians, nurses, and pharmacists
<b>Clinical, Educational, Professional, and Public Resources</b>	
<a href="http://www.palliativedrugs.com">www.palliativedrugs.com</a>	Extensive information on pharmacologic symptom management
<a href="http://www.aahpm.org">www.aahpm.org</a>	American Academy of Hospice and Palliative Medicine (AAHPM): Physician membership organization; board review courses; publications
<a href="http://www.abim.org">www.abim.org</a>	American Board of Internal Medicine: Physician Board Certification
<a href="http://www.nhpco.org">www.nhpco.org</a>	National Hospice and Palliative Care Organization: Nonprofit membership organization representing hospice and palliative care programs and professionals in the United States
<a href="http://www.hpna.org">www.hpna.org</a>	Hospice & Palliative Nurses Association: Specialty nursing organization with evidence-based educational tools for the nursing team
<a href="http://pallcare.hms.harvard.edu">pallcare.hms.harvard.edu</a>	Center for Palliative Care at Harvard Medical School: Faculty development courses, other educational programs
<a href="http://www.nationalcoalitionhpc.org/ncp">www.nationalcoalitionhpc.org/ncp</a>	National Consensus Project for Quality Palliative Care: Clinical practice guidelines
<a href="http://www.americangeriatrics.org">www.americangeriatrics.org</a>	American Geriatrics Society: Clinical guidelines and continuing education
<a href="http://www.cancerpatienteducation.org">www.cancerpatienteducation.org</a>	Cancer Patient Education Network (CPEN): Health care professional organization for sharing experiences and best practices in all aspects of cancer patient education
<b>Palliative Care Program Development</b>	
<a href="http://www.capc.org">www.capc.org</a>	Center to Advance Palliative Care: Technical assistance for clinicians and hospitals seeking to establish or strengthen a palliative care program
<a href="http://www.capc.org/palliative-care-leadership-centers">www.capc.org/palliative-care-leadership-centers</a>	Palliative Care Leadership Centers: Eight exemplary palliative care programs providing site visits, hands-on training, and technical assistance for new palliative care clinicians and programs
<a href="http://aahpm.org/positions/pad">aahpm.org/positions/pad</a>	Statement on Physician-Assisted Dying approved by the AAHPM Board of Directors





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