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# Primary care for the declining cancer survivor

## Asking yourself 1 question can help you to estimate an advanced cancer patient's prognosis and determine how best to help in setting end-of-life priorities.

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**PRACTICE RECOMMENDATIONS**

› *Implement palliative/supportive care shortly after the diagnosis of an incurable cancer.* Ⓐ

› *Candidly communicate prognoses to patients and help them adjust their goals of care.* Ⓑ

› *Recommend hospice care for patients who likely have less than 6 months to live, especially with treatment-related complications or significant caregiver stress.* Ⓑ

› *Delay opioid therapy—if possible—to better control symptoms near the end of life.* Ⓒ

**Strength of recommendation (SOR)**

Ⓐ Good-quality patient-oriented evidence

Ⓑ Inconsistent or limited-quality patient-oriented evidence

Ⓒ Consensus, usual practice, opinion, disease-oriented evidence, case series

As a family physician (FP), you are well positioned to optimize the quality of life of advanced cancer patients as they decline and approach death. You can help them understand their evolving prognosis so that treatment goals can be adjusted, and you can ensure that hospice is implemented early to improve the end-of-life experience. This practical review will help you to provide the best care possible for these patients.

## Family physicians can fill a care gap

The term *cancer survivor* describes a patient who has completed initial cancer treatment. Within this population, many have declining health and ultimately succumb to their disease. There were 16.9 million cancer survivors in the United States as of January 1, 2019,[1] with 53% likely to experience significant symptoms and disability.[2] More than 600,000 American cancer survivors will die in 2019.[3]

In 2011, the Commission on Cancer mandated available outpatient palliative care services at certified cancer centers.[4] Unfortunately, current palliative care resources fall far short of expected needs. A 2010 estimate of required hospice and palliative care physicians demonstrated a staffing gap of more than 50% among those providing outpatient services.[5] The shortage continues,[6] and many cancer patients will look to their FP for supportive care.

FPs, in addition to easing symptoms and adverse effects of medication, can educate patients and families about their disease and prognosis. By providing longitudinal care, FPs can identify critical health declines that oncologists, patients, and families often overlook. FPs can also readily appreciate decline, guide patients toward their care goals, and facilitate comfort care—including at the end of life.

Early outpatient palliative care improves quality of life and patient satisfaction. It also may improve survival time and ward off depression.[7,8] Some patients and providers resist palliative care due to a misconception that it requires abandoning treatment.[9] Actually, palliative care can be given in concert with all active treatments. Many experts recommend a name change from "palliative care" to "supportive care" to dispel this misconception.[10]

### Estimate prognosis using the "surprise question"

Several algorithms are available—using between 2 and 13 patient parameters—to estimate advanced cancer survival. Most of these algorithms are designed to identify the last months or weeks of life, but their utility to predict death within these periods is limited.[11]

The "surprise question" may be the most valuable prognostic test for primary care. In this test, the physician asks him- or herself: Would I be surprised if this patient died in 1 year? Researchers found that when primary care physicians answered No, their patient was 4 times more likely to die within the year than when they answered Yes.[12] This test has a positive predictive value of 20% and a negative predictive value of 95%, making it valuable in distinguishing patients with longer life expectancy.[12] Although it overidentifies at-risk patients, the "surprise question" is a simple and sensitive tool for defining prognosis.

## Priorities for patients likely to live more than a year

For patients who likely have more than a year to live, the focus is on symptom management and preparation for future decline. Initiate and facilitate discussions about end-of-life topics. Cancer survivors are often open to discussions on these topics, which include advanced directives, home health aides, and hospice.[13] Patients can set specific goals for their remaining time, such as engaging in travel, personal projects, or special events. Cancer patients have better end-of-life experiences and families have improved mental health after these discussions.[14] Although cancer patients are more likely than other terminal patients to have end-of-life discussions, fewer than 40% ever do.[15]

Address distressing symptoms with a focus on maintaining function. More than 50% of advanced cancer patients experience fatigue, weakness, pain, weight loss, and anorexia,[16] and up to 60% experience psychological distress.[17] Deprescribing most preventive medications is recommended with transition to symptomatic treatment.[18]

## Priorities for patients with less than a year to live

For patients who may have less than a year to live, focus shifts to their wishes for the time remaining and priorities for the dying process. Most patients start out with prognostic views more optimistic than those of their physicians, but this gap narrows after end-of-life discussions.[19,20] Patients with incurable cancer are less likely to choose aggressive therapy if they believe their 6-month survival probability is less than 90%.[21] Honest conversations, with best- and worst-case scenarios, are important to patients and families, and should occur while the patient is well enough to participate and set goals.[22]

In the last months of life, opioids become the primary treatment for pain and air hunger. As function declines, concerns about such adverse effects as falls and confusion decrease. Opioids have been shown to be most effective over the course of 4 weeks, and avoiding their use in earlier stages may increase their efficacy at the end of life.[23]

## Hospice benefit—more comfort, with limitations

Hospice care consists of services administered by nonprofit and for-profit entities covered by Medicare, Medicaid, and many private insurers.[24] Hospice strives to allow patients to approach death in comfort, meeting their goal of a "good death." A recent literature review identified 4 aspects of a good death that terminally ill patients and their families considered most important: control of the dying process, relief of pain, spirituality, and emotional well-being (**TABLE 1**).[25]

Hospice use is increasing, yet many enroll too late to fully benefit. While cancer patients alone are not currently tracked, the use of hospice by Medicare beneficiaries increased from 44% in 2012 to 48% in 2019.[24] In 2017, the median hospice stay was 19 days.[24]

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**The national shortage of physicians providing outpatient palliative care services is a gap that family physicians should step into.**

**TABLE 1**

## Patient priorities for a "good death"[25]

Findings reported here are based on a systematic review of 20 studies.

| Priority | Studies confirming the priority (%) |
|---|---|
| Control of dying process<br>• Where, how, and who will be there<br>• Dying during sleep<br>• Prepared for death (advanced directives, funeral arranged) | 100% |
| Free of pain and suffering | 85% |
| Religiosity/spirituality<br>• Faith and comfort<br>• Meeting with clergy | 65% |
| Emotional well-being<br>• Emotional support<br>• Psychological comfort<br>• Opportunity to discuss the meaning of death | 60% |
| Life completion<br>• Saying good-bye<br>• Life well lived<br>• Acceptance of death | 55% |
| Treatment preferences<br>• Not prolonging life<br>• Belief that all available treatments were used<br>• Control over treatment | 55% |
| Dignity<br>• Independence<br>• Respected as individual | 55% |
| Family<br>• Family support<br>• Family acceptance and preparedness<br>• Not being a burden | 55% |
| Quality of life<br>• Living as usual<br>• Maintain hope, pleasure, gratitude<br>• Life worth living | 35% |
| Relationship with health care providers<br>• Trust, support, comfort provided<br>• Physician comfort with death<br>• Opportunity to discuss beliefs and fears with physician | 20% |

Unfortunately, though, just 28% of hospice-eligible patients enrolled in hospice in their last week of life.[24] Without hospice, patients often receive excessive care near death. More than 6% receive aggressive chemotherapy in their last 2 weeks of life, and nearly 10% receive a life-prolonging procedure in their last month.[26]

Hospice care replaces standard hospital care, although patients can elect to be followed by their primary care physician.[9] Most hospice services are provided as needed or continuously at the patient's home, including assisted living facilities. And it is also offered as part of hospital care. Hospice services are interdisciplinary, provided by physicians, nurses, social workers, chaplains, and health aides. Hospices have on-call staff to assess and treat complications, avoiding emergency hospital visits.[9] And hospice includes up to 5 days respite care for family caregivers, although with a 5% copay.[9] Most hospice entities run inpatient facilities for care that cannot be effectively provided at home.

**Hospice care has limitations**—many set by insurance. Medicare, for example, stipulates that a primary care or hospice physician must certify the patient has a reasonable prognosis of 6 months or less and is expected to have a declining course.[27] Patients who survive longer than 6 months are recertified by the same criteria every 60 days.[27]

Hospice patients forgo treatments aimed at curing their terminal diagnosis.[28] Some hospice entities allow noncurative therapies while others do not. Hospice covers prescription medications for symptom control only, although patients can receive care unrelated to the terminal diagnosis under regular benefits.[28] Hospice care practices differ from standard care in ways that may surprise patients and families (**TABLE 2**[27,28]). Patients can disenroll and re-enroll in hospice as they wish.[28]

## Symptom control in advanced cancer

### General symptoms

**Pain** affects 64% of patients with advanced cancer.[29] Evidence shows that cancer pain is often undertreated, with a recent systematic review reporting undertreated pain in 32%

**TABLE 2**

### Limitations of hospice

**Medicare limitations**[27,28]

- No therapy with aim of cure
- No medications other than for symptom control
- No outpatient/inpatient care or ambulance services unless prescribed by hospice team
- All care through hospice team, unless unrelated to terminal diagnosis
    - Primary care physician is paid by Medicare if designated by patient
- No room and board coverage except for respite care

**Hospice practice-based limitations that vary but are often in effect**[a]

- No physical therapy services
- No tube feeding
- No intravenous therapies (oral, subcutaneous, sublingual, and rectal dosing used)
- No mechanical ventilation

[a]Based on the authors' experience.

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of patients.[30] State and national chronic opioid guidelines do not restrict use for cancer pain.[31] Opioids are effective in 75% of cancer patients over 1 month, but there is no evidence of benefit after this period.[23] In fact, increasing evidence demonstrates that pain is likely negatively responsive to opioids over longer periods.[32] Opioid adverse effects can worsen other cancer symptoms, including depression, anxiety, fatigue, constipation, hypogonadism, and cognitive dysfunction.[32] Delaying opioid therapy to end of life can limit adverse effects and may preserve pain-control efficacy for the dying process.

Most cancer pain is partially neuropathic, so anticonvulsant and antidepressant medications can help.[33] Gabapentin, pregabalin, and duloxetine are recommended based on evidence not restricted to cancer.[34] Cannabinoids have been evaluated in 2 trials of cancer pain with 440 patients and showed a borderline significant reduction of pain.[35]

Palliative radiation therapy can sometimes reduce pain. Bone metastases pain has been studied the most, and the literature suggests that palliative radiation provides improvement for 60% of patients and complete relief to 25% of patients.[36] Palliative thoracic radiotherapy for primary or metastatic lung masses reduces pain by more than 70% while improving dyspnea, hemoptysis, and cough in a majority of patients.[36]

Other uses of palliative radiation have varied evidence. Palliative chemotherapy has less evidence of benefit. In a recent multicenter cohort trial, chemotherapy in end-stage cancer reduced quality of life in patients with good functional status, without affecting quality of life when function was limited.[37] Palliative chemotherapy may be beneficial if combined with corticosteroids or radiation therapy.[38]

Treatment in the last weeks of life centers on opioids; dose increases do not shorten survival.[39] Cancer patients are 4 times as likely as noncancer patients to have severe or excruciating pain during the last 3 days of life.[40] Narcotics can be titrated aggressively near end of life with less concern for hypotension, respiratory depression, or level of consciousness. Palliative sedation remains an option for uncontrolled pain.[41]

**Anorexia** is only a problem if quality of life is affected. Cachexia is caused by increases in cytokines more than reduced calorie intake.[42] Reversible causes of reduced eating may be found, including candidiasis, dental problems, depression, or constipation. Megestrol acetate improves weight (number needed to treat = 12), although it significantly increases mortality (number needed to harm = 23), making its use controversial.[43] Limited study of cannabinoids has not shown effectiveness in treating anorexia.[35]

**Constipation** in advanced cancer is often related to opioid therapy, although bowel obstruction must be considered. Opioid-induced constipation affects 40% to 90% of patients on long-term treatment,[44] and 5 days of opioid treatment nearly doubles gastrointestinal transit time.[45] Opioid-induced constipation can be treated by adding a stimulating laxative followed by a peripheral acting μ-opioid receptor antagonist, such as subcutaneous methylnaltrexone or oral naloxegol.[46] These medications are contraindicated if ileus or bowel obstruction is suspected.[46]

TABLE 3

## Strategies for preventing delirium near the end of life[48,51]

| | |
|---|---|
| Correct nonmedication cause | Give supplemental oxygen as needed |
| | Treat severe pain |
| | Prevent bladder retention, but minimize catheterization |
| | Ensure bowel function |
| | Encourage mobilization |
| Correct medication cause | Minimize benzodiazepines, anticholinergics, antihistamines |
| | Eliminate drug interactions; dose for renal/hepatic limits |
| Normalize sleep-wake cycle | Have interior lighting follow time of day |
| | Reduce stimulation at night |
| Reorientation | Encourage appropriate use of glasses/hearing aids |
| | Display a clock and other cues of date |
| | Keep communication clear and consistent |
| | Identify staff contacts for continuity/familiarity |
| | Encourage calm reassurance from family members |

**Nausea and vomiting** are common in advanced cancer and have numerous causes. Approximately half of reversible causes are medication adverse effects from either chemotherapy or pain medication.[47] Opioid rotation may improve symptoms.[47] A suspected bowel obstruction should be evaluated by specialists; surgery, palliative chemotherapy, radiation therapy, or stenting may be required. Oncologists can best manage adverse effects of chemotherapy. For nausea and vomiting unrelated to chemotherapy, consider treating constipation and pain. Medication can also be helpful; a systemic review suggests metoclopramide works best, with some evidence supporting other dopaminergic agonists, including haloperidol.[47]

**Fatigue.** Both methylphenidate and modafinil have been studied to treat cancer-related fatigue.[48] A majority of patients treated with methylphenidate reported less cancer-related fatigue at 4 weeks and wished to continue treatment.[49] Modafinil demonstrated minimal improvement in fatigue.[50] Sleep disorders, often due to anxiety or sleep apnea, may be a correctable cause.

### Later symptoms

**Delirium** occurs in up to 90% of cancer patients near the end of life, and can signal death.[51] Up to half of the delirium seen in palliative care is reversible.[51] Reversible causes include uncontrolled pain, medication adverse effects, and urinary and fecal retention (TABLE 3[48,51]). Addressing these factors reduces delirium, based on studies in postoperative patients.[52] Consider opioid rotation if neurotoxicity is suspected.[51]

Delirium can be accompanied by agitation or decreased responsiveness.[53] Agitated delirium commonly presents with moaning, facial grimacing, and purposeless repetitive movements, such as plucking bedsheets or removing clothes.[51] Delirious patients without agitation have reported, following recovery, distress similar to that experienced by agitated patients.[54] Caregivers are most likely to recognize delirium and often become upset. Educating family members about the frequency of delirium can lessen this distress.[54]

Delirium can be treated with antipsychotics; haloperidol has been most frequently studied.[54] Antipsychotics are effective at reducing agitation but not at restoring cognition.[55] Case reports suggest that use of atypical antipsychotics can be beneficial if adverse effects limit haloperidol dosing.[56] Agitated delirium is the most frequent indication for palliative sedation.[57]

**Dyspnea.** In the last weeks, days, or hours of life, dyspnea is common and often distressing. Dyspnea appears to be multifac-

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torial, worsened by poor control of secretions, airway hyperactivity, and lung pathologies.[58] Intravenous hydration may unintentionally exacerbate dyspnea. Hospice providers generally discourage intravenous hydration because relative dehydration reduces terminal respiratory secretions ("death rattle") and increases patient comfort.[59]

Some simple nonpharmacologic interventions have benefit. Oxygen is commonly employed, although multiple studies show no benefit over room air.[59] Directing a handheld fan at the face does reduce dyspnea, likely by activation of the maxillary branch of the trigeminal nerve.[60]

Opioids effectively treat dyspnea near the end of life with oral and parenteral dosing, but the evidence does not support nebulized opioids.[61] Opioid doses required to treat dyspnea are less than those for pain and do not cause significant respiratory depression.[62] If a patient taking opioids experiences dyspnea, a 25% dose increase is recommended.[63]

Anticholinergic medications can improve excessive airway secretions associated with dyspnea. Glycopyrrolate causes less delirium because it does not cross the blood-brain barrier, while scopolamine patches have reduced anticholinergic adverse effects, but effects are delayed until 12 hours after patch placement.[64] Atropine eye drops given sublingually were effective in a small study.[65]

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## Palliative sedation

Palliative sedation can manage intractable symptoms near the end of life. A recent systematic review suggests that palliative sedation does not shorten life.[57] Sedation is most often initiated by gradual increases in medication doses.[57] Midazolam is most often employed, but antipsychotics are also used.[57] JFP

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**Reversible causes of delirium include uncontrolled pain, medication adverse effects, and urinary and fecal retention.**