Improving Patient and Caregiver Outcomes in Oncology: Team-Based, Timely, and Targeted Palliative Care

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Abstract: Over the past decade, a large body of evidence has accumulated supporting the integration of palliative care into oncology practice for patients with advanced cancer. The question is no longer whether palliative care should be offered, but what is the optimal model of delivery, when is the ideal time to refer, who is in greatest need of a referral, and how much palliative care should oncologists themselves be providing. These questions are particularly relevant given the scarcity of palliative care resources internationally. In this state-of-the-science review directed at the practicing cancer clinician, the authors first discuss the contemporary literature examining the impact of specialist palliative care on various health outcomes. Then, conceptual models are provided to support team-based, timely, and targeted palliative care. Team-based palliative care allows the interdisciplinary members to address comprehensively the multidimensional care needs of patients and their caregivers. Timely palliative care, at its best, is preventive care to minimize crises at the end of life. Targeted palliative care involves identifying the patients most likely to benefit from specialist palliative care interventions, akin to the concept of targeted cancer therapies. Finally, the strengths and weaknesses of innovative care models, such as outpatient clinics, embedded clinics, nurse-led palliative care, primary palliative care provided by oncology teams, and automatic referral, are summarized. Moving forward, more research is needed to determine how different health systems can best personalize palliative care to provide the right level of intervention, for the right patient, in the right setting, at the right time. CA: A Cancer Journal for Clinicians 2018;68:356-376. © 2018 American Cancer Society.

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INTRODUCTION

Despite major advances in cancer therapeutics over the past decades, patients with cancer continue to experience significant morbidity and mortality.1 Cross-sectional studies have reported consistently that patients with cancer experience a median of 8 to 12 symptoms, many of which are underdiagnosed and undertreated.2,3 In addition to their physical symptom burden, these patients often have unmet supportive care needs, such as psychological distress, and a need for health information and care planning.4 This supportive care need is further amplified by the finding that the incidence of cancer is increasing worldwide with an aging population and that many patients with advanced cancer are living longer with an incurable illness because of more effective cancer treatments.5 Traditionally, oncologists have played a central role in the delivery of supportive care. Many oncologists see supportive care as an essential component of oncology care and derive satisfaction from providing it.6,7 Working on the front lines of cancer care, oncologists are invariably involved in palliating cancer-related symptoms, managing treatment side-effects, discussing prognosis, facilitating end-of-life discussions, and referring patients to other specialties.8 However, there is significant variation in the provision of supportive care and palliative care referral among oncologists.9,10 The increasingly complex oncology therapeutic landscape,
coupled with busier clinics, means that it is more and more challenging for the oncology team alone to address supportive care needs comprehensively.\textsuperscript{8,11} Meanwhile, the implementation of routine symptom distress screening is uncovering even more supportive care needs among patients with cancer.\textsuperscript{11,12} In addition, supportive care itself is becoming increasingly specialized, with a rapidly growing body of knowledge and research.\textsuperscript{13}

Palliative care has evolved over the last few decades from a philosophy of care for dying patients to a professional discipline with expertise in symptom management, psychosocial and spiritual care, caregiver support, patient-clinician communication, complex decision making, and end-of-life care.\textsuperscript{14,15} It is particularly well positioned to work alongside oncology teams to address the complex supportive care needs of patients with cancer and their families.\textsuperscript{16,17} Importantly, the provision of palliative care should not be limited to the last days or weeks of life, because many of the key domains of care described above can (and should) be provided much earlier in the disease trajectory to improve patient and caregiver outcomes.\textsuperscript{18}

Recognizing the added value of palliative care, many national and international organizations, such as the World Health Organization, the American Society of Clinical Oncology, the American Cancer Society, and the Institute of Medicine, all promote early palliative care involvement alongside standard oncology care.\textsuperscript{19–22} The relevant question is no longer whether palliative care should be offered, but what is the optimal model of delivery, when is the ideal time to refer, who is in greatest need of a referral, and how much palliative care should oncologists be providing, particularly given the scarcity of palliative care resources internationally. In this state-of-the-science review directed at the practicing oncology clinician, we: 1) discuss the contemporary literature examining the impact of palliative care on care outcomes; 2) provide conceptual frameworks on interdisciplinary, timely, and targeted palliative care; and 3) summarize the strengths and weaknesses of innovative care models, such as outpatient clinics, embedded clinics, nurse-led palliative care, primary palliative care provided by oncology teams, and automatic referral.

Summary/Key Points

- The growing number of patients living longer with advanced cancer, coupled with heightened awareness of distress through routine symptom screening, translates into an increasing demand for supportive care.
- Palliative care is a professional discipline that is well positioned to work together with the oncology team to support the physical, emotional, social, spiritual, informational, and decision-making needs of patients with cancer and their families throughout the disease trajectory.

EVIDENCE TO SUPPORT EARLY PALLIATIVE CARE

Randomized Controlled Trials

Over the past decade, there has been an explosion of clinical trials comparing concurrent oncologic and palliative care versus usual oncologic care alone in outpatient and inpatient settings, providing level 1 evidence to support the integration of palliative care along the disease trajectory.\textsuperscript{23–40} In this section, we focus on more recent publications, because older studies have been summarized in previous reviews.\textsuperscript{18,41–43} Table 1 highlights the key elements of study design and outcomes.\textsuperscript{23–40,44} A majority of these clinical trials concluded that concurrent palliative care improves quality of life, symptoms, and patient-clinician communication compared with oncologic care alone.\textsuperscript{25,26,29,31,37,39,44} Some studies also demonstrated that palliative care enhances mood, patient satisfaction, quality of end-of-life care, survival, and caregiver outcomes (Table 1).\textsuperscript{23–40,44} Of note, none of the studies favored oncologic care alone for the primary outcome.

It is noteworthy that there is heterogeneity in trial design among the clinical trials, with variable inclusion criteria, care settings, outcome measures, and timing of assessment. These differences in design, combined with significant differences in the nature of palliative care interventions and the timing and intensity of care delivery, contributed to the variability in study outcomes (Table 1).\textsuperscript{25,26,29–31,33–39,44} Although the diversity in trial design makes it more difficult to assess the magnitude of benefit associated with palliative care, it also provides a unique opportunity to ascertain which aspects of palliative care may be most beneficial, particularly concerning the level of comprehensiveness of the palliative care service and the timing of referral.

Palliative care is a highly complex, multidimensional intervention, making it difficult to standardize. Although efforts have been made to define the key domains of palliative care,\textsuperscript{14,15} it is less clear who is positioned best to deliver palliative care and how comprehensive the team should be. Furthermore, palliative care has not yet been accredited in some countries, which may contribute further to inconsistencies in its delivery. As shown in Table 1, it appears that studies involving interdisciplinary palliative care teams were more likely to have a positive outcome than those involving nurse-led palliative care (4 of 5 trials vs 2 of 6 trials for the primary outcome).\textsuperscript{23–40,44} However, to date, no single study has directly compared interdisciplinary teams...
| STUDY                        | WHO (ADVANCED) | WHEN            | WHERE         | WHAT                      | QUALITY OF LIFE | SYMPTOMS | MOOD     | SATISFACTION | COMMUNICATION | EOL CARE | SURVIVAL | CAREGIVERS |
|-----------------------------|----------------|-----------------|---------------|---------------------------|----------------|----------|----------|--------------|---------------|----------|----------|------------|
| Temel 2011,23 Greer 2012,24 | Lung           | Within 8 wk of diagnosis | USA | Outpatient-based | Favors PC     | Favors PC |        | Favors PC     | Favors PC     | Favors PC | Favors PC |            |
| Zimmerman 201425           | Breast, lung, GI, GU, GYN | Prognosis 6-24 mo | Canada | Outpatient-based | Favors PC     | Favors PC | Favors PC | Favors PC     | Favors PC     |          |          |            |
| Temel 2016,26 El-Jawahri 2017 | Lung, GI      | Within 8 wk of diagnosis | USA | Outpatient-based | Favors PC     | Favors PC |        | Mixed findings | Mixed findings |          |          |            |
| Maltoni 201628,29           | Pancreas       | Within 8 wk of diagnosis; prognosis >2 mo | Italy | Outpatient-based | Favors PC     |        | Did not differ | Mixed findings | Did not differ |          |          |            |
| Groenvold 201730            | Solid tumors   | Symptomatic based on EORTC-QLQ-C30 | Denmark | Outpatient-based | Mixed findings |        |        | Mixed findings | Did not differ |          |          |            |
| Nurse-led PC                |                |                 |               |                           |                |          |          |              |               |          |          |            |
| Bakitas 2009,31 Dionne-Odom 2016 | Breast, lung, GI, GU | Within 8-12 wk of diagnosis | USA | APN-led, phone based | Favors PC     | Did not differ | Favors PC | Did not differ | Mixed findings |          |          |            |
| Dyar 201233                 | Solid tumors   | Likely to be referred to hospice within the next 12 mo | USA | APN embedded in oncology | Mixed findings | Mixed findings |        | Did not differ | Did not differ |          |          |            |
| Tattersall 201434           | Solid tumors   | Newly diagnosed metastatic disease; prognosis <12 mo | Australia | RN-led | Did not differ | Mixed findings | Did not differ | Did not differ | Did not differ |          |          | Favors no PC |
| McCorkle 201535             | Not clearly specified | Within 100 d of diagnosis | USA | APN-led | Did not differ | Did not differ |        |            |            | Favors PC |          |            |
| Bakitas 201536              | Solid and hematologic malignancies | Within 1-2 mo of diagnosis; prognosis <12 mo | USA | APN-led, phone based | Did not differ | Did not differ | Did not differ | Did not differ | Did not differ | Favors PC |          |            |
| Vanbutsele 201837          | Solid tumors   | Within 12 wk of diagnosis or recent progression; prognosis <12 mo | Belgium | RN-led OP team | Favors PC     | Did not differ | Did not differ | Did not differ | Mixed findings |          |          |            |
| Inpatient                   |                |                 |               |                           |                |          |          |              |               |          |          |            |
| Grudzen 201630              | Solid and hematologic malignancies | On admission | USA | IP team | Favors PC     | Did not differ | Did not differ | Did not differ | Did not differ |          |          |            |
| El-Jawahri 2016,39 201740   | Stem cell transplantation | On admission | USA | IP team | Favors PC     | Favors PC     | Favors PC | Favors PC     | Favors PC     |          |          | Mixed findings |

Abbreviations: APN, advanced practice nurse; EOL, end of life; EORTC-QLQ-C30, European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire; GI, gastrointestinal; GU, genitourinary; GYN, gynecologic; IP, inpatient; OP, outpatient; PC, palliative care; RN, registered nurse.

*The outcomes are color coded to facilitate interpretation. Green = favored the palliative care group with statistically significant findings; light green = some outcomes significantly favored palliative care group, other outcomes equivocal; orange = no statistically significant difference between the palliative care group and the usual oncologic care group; red = favored the usual oncologic care group with statistically significant findings.
| META-ANALYSIS | SETTING | NO. OF STUDIES | NO. OF PATIENTS | QUALITY OF LIFE | SYMPTOMS | MOOD | SURVIVAL | OTHER OUTCOMES |
|--------------|---------|----------------|----------------|----------------|----------|------|----------|----------------|
| Kavalieratos 2016 | Cancer and noncancer | 15 | 2355 | Favors PC; SMD, 0.46; 95% CI, 0.08-0.83 | Favors PC; SMD, −0.66; 95% CI, −1.25 to −0.07 | Did not differ; SMD, −0.39 to 0.01 | Did not differ; HR, 0.90; 95% CI, 0.69-1.1 | PC was associated consistently with improvements in advance care planning, patient and caregiver satisfaction, and lower health care utilization |
| Gartner 2017 | Cancer and noncancer | 12 | 2454 | Favors PC; SMD, 0.16; 95% CI, 0.01-0.31 | Did not differ; SMD, −0.38; 95% CI, −0.82 to 0.06 | Did not differ; SMD, −0.21; 95% CI, −1.35 to 0.94 | Did not differ; HR, 0.82; 95% CI, 0.60-1.13 |
| Haun 2017 | Advanced cancer | 7 | 1614 | Favors PC; SMD, 0.27; 95% CI, 0.15-0.38 | Favors PC; SMD, −0.23; 95% CI, −0.35 to −0.10 | Did not differ; SMD, −0.11; 95% CI, −0.26 to 0.03 | Did not differ; HR, 0.85; 95% CI, 0.56-1.28 | RCTs on professional PC services that provided or coordinated comprehensive care for adults at early advanced stages of cancer |

Abbreviations: 95% CI, 95% confidence interval; HR, hazard ratio; PC, palliative care; SMD, standardized mean difference; RCTs, randomized controlled trials.

The outcomes are color coded to facilitate interpretation. Green = favored the palliative care group with statistically significant findings; orange = no statistically significant difference between the palliative care group and the usual oncologic care group.
with single-practitioner–led models, and further research is needed.

Although earlier referral to palliative care is considered to be better than late referral, the optimal timing of referral has not yet been defined. To date, only one randomized clinical trial (RCT) has attempted to address this question directly. By using a wait-list design, the Project ENABLE III study compared early palliative care (within 8 to 12 weeks of diagnosis) versus delayed (3 months later). The primary outcome was measured at 3 months. The investigators also conducted longitudinal analyses and reported no significant difference between the 2 groups in quality of life. However, that study had several limitations complicating its interpretation, including underenrollment and contamination. Moreover, the study intervention was predominantly nurse-led and telephone-based, with referral to an interdisciplinary palliative care team on an as-needed basis. Studies that used other designs to address the optimal timing of referral are discussed below.

**Meta-Analyses**

Summarizing data from the aforementioned trials and others, 3 meta-analyses were published in 2016 of 2017 on the impact of palliative care on health outcomes (Table 2).

All 3 concluded that palliative care was associated with improved quality of life, albeit with a small effect size; 2 also concluded that palliative care was associated with improved symptom control, none reported a significant improvement in survival. This small observed benefit may be because the studies included in the meta-analyses mostly had small effect sizes and also included trials with variable designs. One study further concluded that earlier palliative care was associated with a greater quality-of-life benefit, although that subgroup analysis included only 6 studies (2 studies of early palliative care and 4 studies of nonearly palliative care).

In addition to the heterogeneity among clinical trials, the 3 meta-analyses used different eligibility criteria, resulting in the inclusion of different trials and somewhat variable findings. The review by Kavalieratos et al had the broadest inclusion criteria, including 43 trials in patients with life-limiting illness, for which interventions comprised at least 2 of 8 possible domains of palliative care, as defined by the National Consensus Project for Quality Palliative Care. Palliative care was associated with a statistically and clinically meaningful improvement in quality of life overall for the 15 studies included in one meta-analysis, but not when patients with (or without) cancer were analyzed in isolation. The review by Gaertner et al included 10 trials of patients with any advanced illness in which the intervention was a multiprofessional palliative care team and reported a marginally larger effect of palliative care on quality of life in patients with cancer than in those without cancer. The review by Haun et al included 7 cancer trials that specifically assessed the effects of early palliative care intervention, concluding that quality of life was better in patients with cancer who received early palliative care. Ultimately, these meta-analyses underscore the need to conduct further research to identify the optimal model(s) of palliative care delivery in different settings.

**Cost Benefits**

In addition to improved patient and caregiver outcomes, palliative care is also associated with reduced health care costs. In part, this is driven by the tendency of palliative care teams to minimize investigations, interventions, and hospitalizations at the end of life that not only have questionable benefits but also are expensive. Morrison et al reported that an inpatient palliative care consultation was associated with significant cost savings compared with no palliative care, supporting the economic benefit of palliative care for third-party payers and institutions under the Diagnostic Related Grouping payment system. Smith et al conducted a systematic review of 46 studies and concluded that palliative care was consistently less costly relative to comparator groups. Another systematic review in 2018 reported that a palliative care consultation within 3 days of admission for patients with cancer was associated with a reduction in total direct hospital cost by $4251 (95% confidence interval, $3837–$4664) per hospitalization. More high-quality studies are needed to investigate the economic impact from the perspective of different payers (eg, government, insurers, third-party organizations, patients, and family caregivers), in different settings (eg, outpatient, inpatient, home care), and with different models of palliative care (eg, comprehensive teams vs nurse-led care).

**Summary**

- Most RCTs demonstrate that palliative care combined with oncologic care improves quality of life and symptom control.
- Clinical trials involving interdisciplinary palliative care teams, instead of nurse-led palliative care, appear to be more likely to be associated with positive findings.
- Three recent meta-analyses concluded that palliative care was associated with improved quality of life. However, the effect size was small, which may be related to heterogeneity in trial design.
- A meta-analysis examining the timing of palliative care referral supported that earlier referral was associated with greater benefits on quality of life.
- Palliative care can improve health care value by reducing...
costly investigations, interventions, and hospitalizations at the end of life, especially those with questionable benefits.

**DEFINING KEY ELEMENTS OF PALLIATIVE CARE DELIVERY: TEAM-BASED, TIMELY, AND TARGETED CARE**

Our critical appraisal of contemporary RCTs above supports the association between specialist palliative care and improved outcomes. Efforts are currently underway to identify the “active ingredients” in this complex intervention and to help standardize the delivery of palliative care. In the section below, we use conceptual frameworks to discuss 4 key questions: What is the right service model? When is the right time? Who is the right patient? And how much palliative care should oncologists provide?

**What Is the Right Service Model? The Role of Team-Based Palliative Care**

One of the most unique and fundamental aspects of palliative care is its interdisciplinary nature, which allows the team to deliver multidimensional care addressing the complex supportive care needs of patients with advanced cancer. Figure 1 illustrates the interconnectedness of the supportive care needs of patients with advanced cancer. One of the strengths of this interdisciplinary palliative care approach is the shared decision making, responsibility, and leadership to support patients and families. The physician, nurse, psychologist, social worker, chaplain, pharmacist, physiotherapist, occupational therapist, and other allied health professionals each contribute their unique expertise while working together in a cohesive manner to support the patient’s goals of care through impeccable assessments, coordinated communication, and multidimensional interventions (Fig. 2). Not all members are required at all times—some may be needed more often than others, and some may form a closer relationship with the patient. In a secondary analysis of the trial by Temel et al., Hoerger et al reported that patients who had a greater proportion of visits focused on coping, treatment decisions, and advance care planning (ACP) had better outcomes related to quality of life, chemotherapy use at the end of life, and hospice utilization, respectively, suggesting that each component of palliative care has a specific and complementary purpose. Although this interprofessional approach is particularly useful in addressing intense care needs at the end of life, it is also appropriate for patients earlier in the disease trajectory. For example, an interdisciplinary intervention may be particularly helpful to support patients with cancer who are at risk of opioid misuse. This teamwork may also help to reduce burnout among palliative care clinicians, which represents an area for future research. An international Delphi study in 2015 reached consensus that, at a minimum, interdisciplinary teams should consist of a physician, nurse, and psychosocial team member. The interdisciplinary team may be led by a physician, nurse, or another discipline, with situational leadership depending on the care needs.

On the basis of the conceptual framework and evidence presented above, models of palliative care involving predominantly a single profession may not be able to support patients who have more complex care needs as comprehensively. For example, there is much variation in the intensity of interdisciplinary palliative care involvement among the nurse-led palliative care trials (Table 1), although they generally involved a nurse providing palliative care education/support in the front line, with referral to specialist palliative care teams on an as needed basis. Studies with limited longitudinal interdisciplinary palliative care engagement often had negative outcomes. Properly designed and incorporated, nurse-led interventions may augment the basic level of primary palliative care provided by oncologists, with specialist palliative care reserved for patients in greater distress. Although single disciplinary palliative care should not replace specialist palliative care teams, it may have a role in resource-limited settings, such as rural areas or developing regions. Further research is needed to identify the right intervention for the right setting.
FIGURE 2. The Interdisciplinary Palliative Care Team. One of the most unique aspects of palliative care is its interdisciplinary nature, with different members of the team providing different expertise, thus allowing a patient's needs to be addressed in a holistic and timely fashion, and augmenting the ability of family caregiver(s) to support the patient. Other advantages of an interdisciplinary team include enhanced patient-clinician communication and shared responsibility, work load, decision making, leadership, and stresses while providing care for distressed patients.

FIGURE 3. Conceptual Framework on How Timely Palliative Care Can Impact Patient Outcomes. This conceptual model highlights that there may be multiple mechanisms by which palliative care can improve each outcome. An anticipatory approach to symptom management would allow patients to reduce their symptom burden related to cancer or cancer treatments (Tx), minimize symptom crises, and potentially tolerate cancer treatments better. These, in turn, may help to improve quality of life (QOL) and the quality of end-of-life (EOL) care (eg, avoiding emergency room visits). Longitudinal psychosocial support can improve emotional and spiritual well-being, which also have been associated with patient outcomes downstream. Enhanced communication over time also may assist palliative care teams to improve their understanding of illness and facilitate advance care planning, which could allow patients to minimize aggressive end-of-life care. It remains unclear whether palliative care can have a survival benefit. Some investigators have postulated that a survival benefit from palliative care may be related to better management of depression, although palliative care also may improve survival by providing good symptom control and reducing intensive care at the end of life that sometimes may be detrimental to survival.³⁸
When Is the Right Time? The Rationale for Timely Palliative Care

Although referrals to palliative care often occur at times of crisis (eg, end of life), palliative care is most effective when introduced early. Figure 3 illustrates some postulated mechanisms with which timely palliative care can improve various patient-related outcomes. Appropriate and timely symptom interventions, patient education, and side-effect management may help to minimize emergency room visits and hospitalizations while maximizing patients’ function. Longitudinal counseling can help to enhance coping strategies in times of stress. Prospective observational studies and RCTs have shown that serious illness conversations, ACP, spiritual care, and improved prognostic understanding can help reduce aggressive care at the end of life; all of these are longitudinal processes that require adequate lead-time. By facilitating ACP and providing community-based services, palliative care can support individuals who wish to die at home.

The optimal timing of specialist palliative care referral remains unclear but likely depends on the individual patient and the health care system. In addition to a meta-analysis suggesting that earlier referral was associated with a greater benefit, several nonrandomized studies have also demonstrated the impact of timely palliative care on aggressiveness of care at the end of life. In a retrospective cohort study, patients who were referred to a comprehensive cancer center more than 6 months before death were compared with those who were referred 6 months or less before death. Earlier referrals were associated with significantly better outcomes in the last 30 days of life, with lower rates of emergency room visits (41% vs 63%; \( P = .002 \)) and hospitalizations (51% vs 75%; \( P < .001 \)). Jang et al conducted a population-based study to examine the impact of palliative care on aggressiveness of end-of-life care for 5381 patients with advanced pancreatic cancer. Palliative care involvement was associated with less aggressive care, as measured by the use of chemotherapy near death (odds ratio [OR], 0.34), intensive care unit admissions (OR, 0.12), emergency room visits (OR, 0.19), and hospitalizations near death (OR, 0.24); moreover, earlier palliative care was associated with better outcomes. Studies from Italy and the United Kingdom examining the effect of palliative care confirmed similar benefits with earlier referral.

Although early palliative care referral is generally preferred, some investigators have speculated whether it is ever too early. Many contemporary RCTs involved specialist palliative care referral within 3 months of diagnosis of advanced cancer regardless of symptom burden; however, this model of care is currently infeasible given the limited palliative care infrastructure internationally. Furthermore, some patients with advanced cancer may have limited supportive care needs around the time of diagnosis and may not require palliative care. Thus, instead of early palliative care for all, we advocate for timely palliative care, selecting the

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### TABLE 1: Components of Preventative Care

| Key Aspects                                                                 | Example 1 | Example 2 |
|----------------------------------------------------------------------------|-----------|-----------|
| **Insight into Illness**  
  - Natural history  
  - Prognostication                                                            | Stage IV pancreatic cancer = symptoms | Stage IV lung cancer = short prognosis |
| **Foresight for Individual**  
  - Anticipate concerns  
  - Risk factors                                                              | Mild pain now can get worse | Patient will deteriorate |
| **Interventions Available**  
  - Risk reduction  
  - Evidence-based                                                             | Opioids can be useful | Serious illness conversations |
| **Introduce Intervention**  
  - Timely initiation  
  - Longitudinal followup                                                      | Start scheduled opioids  
  Educate and monitor | Prognostic discussions  
  Advance care planning |
| **Crisis Prevention**  
  - Improved outcomes  
  - Preparations in place                                                     | Better quality of life  
  Avoid pain crisis | Better quality of EOL  
  Avoid ICU visit |

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**FIGURE 4.** Palliative Care Is Preventive Care. By seeing patients in a timely fashion, anticipating care needs, and providing effective interventions through education and longitudinal monitoring, the palliative care team can potentially prevent symptom crises, avoidable hospitalizations, information gaps, and catastrophes at the end of life (EOL) (eg, intubation at an intensive care unit [ICU]).
Palliative Care for Cancer Patients

One approach to determining the right time involves a Delphi consensus. In one study, 60 international experts were asked about the appropriate time to refer patients with advanced cancer to outpatient palliative care. A consensus was defined a priori, with at least 70% of experts reaching agreement. The timing of referral was assessed from 4 different angles: prognosis, time from diagnosis, treatment trajectory, and performance status. Most experts considered that greater than 24 months was too early and identified the optimal timing as a prognosis of 6 to 24 months. Similarly, the ideal timing for referral was within 3 months of diagnosis of advanced cancer if patients had a median survival of 1 year or less, had progressed through at least a single line of systemic therapy, and had an Eastern Cooperative Oncology Group performance of 2 or greater (Fig. 5). A survey asked patients with advanced cancer who were referred to outpatient palliative care about their opinion regarding the optimal timing of referral. The median survival was 8.5 months, and a majority (n = 144; 72%) reported that the timing of referral was appropriate, with 42 (21%) perceiving that the referral was too late and only 14 (7%) feeling that it was too early.

Timely palliative care is best delivered in the outpatient setting, where patients can receive proactive rather than reactive care. The strengths and weakness of various models of palliative care delivery in the outpatient setting are discussed below.

Who Is the Right Patient? A Targeted Approach to Referral

There is currently a gap between the research literature, which recommends routine early palliative care referral, and the reality of clinical practice. If we apply the eligibility criteria in RCTs strictly and adhere to the 2017 American Society of Clinical Oncology guideline, patients with advanced cancer would be referred regardless of symptom burden as long as they meet predefined, time-based criteria (eg, time from diagnosis and/or prognosis) (Table 1), resulting in universal early referral (Fig. 6A). In contrast, oncologists often refer patients selectively based on care needs, which may be delayed because of the underdetection of symptoms and lack of standardized need-based criteria (Fig. 6B).
The optimal model may be a combination of these 2 extremes, with the use of standardized need-based criteria to trigger a referral for patients who are most appropriate for specialist palliative care in the outpatient setting (Fig. 6C). Similar to cancer-targeted therapy, in which tumors with particular mutations are most likely to respond, palliative care is likely to confer the greatest benefit for patients experiencing or anticipated to have high symptom intensity or other supportive care needs. This would allow for a more personalized approach, matching the scarce palliative care resources to the needs of the individuals. The literature to support this more targeted approach is still emerging. Groenvold et al enrolled patients with solid tumors who were symptomatic based on the European Organization for Research and Treatment of Cancer Core 30 Quality-of-Life questionnaire. Although the primary outcome (ie, the most severe European Organization for Research and Treatment of Cancer Core 30 Quality-of-Life symptom item) had greater improvement with palliative care than with usual care, this did not reach statistical significance. Interpretation of the study is complicated because the responsiveness to change of this primary outcome is not well defined. Secondary analysis of other completed RCTs may provide further insights.

**How Much Palliative Care Should Oncologists Provide? The Role of Primary Palliative Care**

Although oncologists always have a role in the provision of palliative care, one key question is how much they should reasonably be expected to provide. Conceptually, palliative care can be categorized into 3 levels based on expertise (Fig. 7). Primary palliative care is basic palliative care provided by the oncology team and primary care physicians; secondary palliative care is defined as specialist palliative care teams working as consultants to address the more complex supportive care needs; and tertiary palliative care involves palliative care as the attending team providing intensive supportive care for the most...
complex patients, such as in an acute palliative care unit. The introduction of nurse-led palliative care models, with an advance practice nurse embedded into an oncology practice, blurs the division between primary and secondary palliative care.

RCTs to date have demonstrated clearly that secondary palliative care integrated with primary palliative care is superior to primary palliative care alone (Tables 2 and 3). However, in resource-restricted circumstances, a fully integrated approach may not be feasible, and a solo practice model in which the oncologist assumes all aspects of supportive/palliative care may be the only option. Even under a fully integrated model, oncologists are expected to provide primary palliative care and address basic supportive care needs in the front line, partly because there is an insufficient palliative care workforce to support all patients who have advanced cancer and/or significant symptom burden. Previous studies revealed that, although a majority of oncologists believe that they are responsible for providing primary palliative care, their levels of confidence and interest vary widely. For example, solid tumor oncologists perceived themselves as more comfortable with the provision of supportive care than hematologic oncologists (P = .003). Primary palliative care delivery by oncologists can also be assessed indirectly by the extent of palliative care education and their knowledge base. Currently, only 20% to 25% of medical oncology fellowship programs in the United States have mandatory palliative care rotations. Furthermore, a majority of medical oncology fellows had difficulty with opioid rotation and desired more palliative care education.

Several groups have undertaken efforts to standardize primary palliative care competencies. This should start with routine systematic screening, basic management of acute or common issues, and recognition of when a patient needs to be referred to specialized services. Standardized referral criteria may further streamline this process and are discussed below. It is also important to differentiate palliative care issues from other supportive care needs best managed by oncologists or other specialists, such as immunotherapy-related toxicities and thromboembolism. More research is needed to define the core competencies and best approaches to educating the next generation of oncologists.

Summary/Key Points

- The interconnectedness of symptoms and supportive care needs necessitates a comprehensive interdisciplinary team to provide multidimensional care.
- Although interdisciplinary palliative care teams are ideal, single-disciplinary palliative care may have a role in the provision of primary palliative care, particularly in resource-limited settings.
Palliative care is most effective as a preventive measure when it is introduced early in the disease trajectory. Its roles in this setting include patient education, proper symptom management, longitudinal counseling and spiritual care, enhancing illness understanding, and ACP.

Timely palliative care is associated with improved quality of life and end-of-life care.

Because of scarce health care resources, it is impossible for all patients to be seen by palliative care from the time of diagnosis. Similar to cancer targeted therapy, a more personalized approach to refer patients with higher current or anticipated supportive care needs may result in better outcomes.

Oncologists have an important role in providing primary palliative care, which includes basic symptom assessment.

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**TABLE 3. Stregths and Weaknesses of Innovative Care Models**

| MODELS                          | POTENTIAL STRENGTHS                                                                                                                                                                                                 | POTENTIAL WEAKNESSES                                                                                                                                                                 |
|---------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Freestanding clinics            | • Strong evidence base                                                                                                                                                                                            | • More startup costs, overheads, and budgetary considerations                                                                                                                       |
|                                 | • Centralized services                                                                                                                                                                                            | • Developing positive collaborative relationships with the oncology team may require greater attention                                                                             |
|                                 | • Allows for more consistent day-to-day planning and resource utilization                                                                                                                                          | • More clinic appointments for patients                                                                                                                                              |
|                                 | • Autonomy around clear and consistent referral criteria                                                                                                                                                          |                                                                                                                                                                                     |
|                                 | • Customized space for patients with advanced disease                                                                                                                                                             |                                                                                                                                                                                     |
|                                 | • Site for education and research in palliative medicine                                                                                                                                                           |                                                                                                                                                                                     |
|                                 | • Greater scope for expansion                                                                                                                                                                                     |                                                                                                                                                                                     |
|                                 | • Visible “home” for the palliative care ambulatory service                                                                                                                                                       |                                                                                                                                                                                     |
| Embedded clinics                | • Immediate access to palliative care team                                                                                                                                                                       | • Difficult to predict volumes and staffing needs from day to day                                                                                                                                 |
|                                 | • Minimizes trips to hospital and wait times                                                                                                                                                                      | • Follow-up visits may be challenging to schedule if needed for palliative care but not oncology                                                                               |
|                                 | • May facilitate collaboration (clinical and research) between oncology and palliative care teams                                                                                                                                 | • Limited scope for expansion                                                                                                                                                         |
|                                 | • May help to destigmatize referral                                                                                                                                                                                | • Typically room only for a single discipline                                                                                                                                         |
|                                 | • Cost-effective in early development of palliative care (shared space, support staff, and other resources)                                                                                                | • Consultation may be rushed and completed in a cramped environment                                                                                                                   |
| Nurse-led practitioners         | • Capacity to engage in oncology rounds and to foster stronger communication between services                                                                                                                    | • Patient and family may be fatigued due to adding on another appointment                                                                                                              |
|                                 | • Nurse education and mentoring role                                                                                                                                                                               | • Providing care across multiple clinics simultaneously may fragment or overstretches services                                                                                |
|                                 | • May be more financially viable than a physician-led model                                                                                                                                                       | • Limited evidence base                                                                                                                                                              |
| Palliative care delivered by    | • Immediate attention to symptom management concerns                                                                                                                                                              | • Reimbursement for nurses                                                                                                                                                            |
| oncology teams                  | • Care delivered longitudinally from diagnosis to death by the oncology team                                                                                                                                      | • A single practitioner cannot replicate the multidisciplinary team involved in holistic palliative care provision          |
|                                 | • Necessary when access to palliative care services limited                                                                                                                                                       | • It may be difficult to staff multiple clinics with palliative care nurses in larger centers                                                                               |
|                                 |                                                                                                                                                                                                                     | • Mixed evidence base and highly heterogeneous models of delivery                                                                                                                   |
| Automatic referral              | • Standardizes the referral process across clinicians                                                                                                                                                              |                                                                                                                                                                                     |
|                                 | • Normalizes the referral process                                                                                                                                                                                  |                                                                                                                                                                                     |
|                                 | • Results in more appropriate referrals, with specialized services provided for those with greatest need                                                                                                         |                                                                                                                                                                                     |
|                                 | • Optimizing health care resource utilization by aligning scarce palliative care resource to patients most in need                                                                                                  |                                                                                                                                                                                     |

Limited evidence for choice of screening tool, cutoff points for referral

Lack of buy-in from patients and/or clinicians may result in low screening rates

May trigger unnecessary referrals for symptoms that are transient or could be managed by oncology team
and treatment, communication, decision making, and referral to specialist palliative care.

INNOVATIVE MODELS OF CARE DELIVERY

The evidence for timely involvement of palliative care and key elements in its delivery are described above. Here, we examine the components of innovative care models for palliative care delivered in the outpatient setting, with an emphasis on highlighting their strengths and limitations. These include freestanding outpatient clinics, palliative care consultants embedded within oncology clinics, nurse practitioner consultants, automated referral to palliative care, and primary palliative care delivered by oncology teams alone (Table 3).

Outpatient Clinics

Timely, integrated palliative care requires contact with patients who have advanced cancer at a time when they remain ambulatory, functionally independent, and engaged with their oncology team in active anticancer treatment. Outpatient clinics provide an ideal setting within which to build trusting relationships with patients and their families, optimize symptom control issues in a timely manner, and explore ACP in a structured, longitudinal fashion in tandem with changes to the patients’ cancer treatment plan.

In 2009, 59% of National Cancer Institute designated cancer centers and 22% of non-National Cancer Institute-designated cancer centers reported having outpatient palliative care clinics in the United States; this proportion has likely grown over time. Several centers have published their experience with freestanding outpatient clinics. In most cases, these clinics have begun as single, one-half–day clinics per week and have grown quickly with increasing demand. Large cancer centers, such as The University of Texas MD Anderson Cancer Center and the Princess Margaret Cancer Center, have clinics that operate daily and offer both booked and urgent same-day appointments. Typically, the core team members providing expertise in the clinic are palliative care physicians and nurses, with other interdisciplinary team members (including social workers, psychologists, spiritual care workers, pharmacists, dieticians, wound care specialists, and occupational and physiotherapists) offering input as required. Referrals are received and booked centrally and can be coordinated with oncology clinic visits if that is the patient’s preference.

There is strong evidence demonstrating the benefits of stand-alone clinics. Patients whose initial palliative care contact was in these clinics have improved outcomes related to aggressiveness of care at the end of life (characterized by fewer prolonged hospitalizations, intensive care unit admissions, and emergency department visits in the last month of life and lower rates of in-hospital death) compared with patients seen by the palliative care team as inpatients. Robust evidence from several large-scale RCTs has demonstrated clear benefits for patients in terms of improved quality of life, symptom management, caregiver distress, and overall survival.

In addition, stand-alone clinics offer several advantages (Table 3). They allow for the centralization of interdisciplinary services, with an organized triage process. This allows for better day-to-day planning and efficient use of the multidisciplinary team, which is particularly important with large-volume services and for teams in which members simultaneously cover inpatient and outpatient palliative care services. Clear referral criteria are set, prioritizing urgent same-day referrals for patients with physical or psychological distress. The clinic itself may be customized for patients who have complex care needs, with low examining tables, a waiting room (or lack thereof) with an emphasis on privacy, ambient music, and standardized comprehensive palliative care assessments. Moreover, the clinic can serve as a specialized setting for education and research. This model also solidifies the independent role played by palliative care teams in cancer care rather than being seen as an appendage of individual oncology clinics. To prevent symptom crises proactively, a centralized clinic may also facilitate the coordination of telehealth interventions.

The main limitations of freestanding outpatient clinics are budgetary and funding restrictions. Consideration needs to be given to this from the outset, with a strong business model and planning for additional resources, space, and clinicians over time. In small centers, it may not be possible to allocate separate space to a clinic that only runs once weekly. Developing positive relationships with referring oncologists may require greater attention compared with embedded clinics. Thus, this model is best suited for large cancer centers with an established palliative care program.

Embedded Clinics

Outpatient palliative care clinics also may be embedded directly within oncology clinics. A few studies have described successful examples of embedded clinics. In one, a palliative care clinic consisting of a physician and a fellow within a private oncology clinic provided one-half–day per week of consult support. This improved symptom burden and increased referral rates by 87% over a 2-year period; each consultation was estimated to save up to 170 minutes of the referring oncologist’s time. Both oncologists and palliative care physicians reported
that the close proximity to one another facilitated better integration of practices.\textsuperscript{105} Cassel et al reported that a palliative care physician within oncology clinics in a rural setting was associated with high levels of patient, family, and referring physician satisfaction.\textsuperscript{106} In a retrospective cohort study, Einstein et al reported their experience embedding a physician and a chaplain weekly into an oncology clinic that specialized in targeted and immune-based therapies.\textsuperscript{107} Patients under the embedded model (n = 26) were more likely than those outside of the embedded clinic (n = 88) to be seen by palliative care for longer periods (173 vs 61 days; \(P < .001\)) and to be referred to hospice earlier (34 vs 10 days; \(P = .006\)).

Embedded clinics offer some advantages both clinically and practically (Table 3). They allow for direct access to the palliative care team, and they minimize the number of hospital trips\textsuperscript{108} and wait times for patients.\textsuperscript{17} In contrast to stand-alone clinics,\textsuperscript{109} embedded clinics also may help to minimize stigma by offering palliative care in the same location as standard oncology care. Embedded clinics may foster improved face-to-face communication and collaboration between oncology and palliative care teams,\textsuperscript{75,108,110} which may spur educational and research opportunities.\textsuperscript{75} Support staff may be shared between the oncology and palliative care services in an embedded model, again allowing for more cohesive care\textsuperscript{110} and cost effectiveness. This may be particularly advantageous for newly established palliative care teams that have limited budgets.\textsuperscript{100}

Conversely, this model also has important limitations. Space limitations restrict involvement of the palliative care team to a single discipline, typically a sole physician or nurse, and limit the possibility of expansion.\textsuperscript{75,105,106} Patients with advanced cancer may not wish to add an additional consultation onto their existing oncology appointment because of lack of time or energy.\textsuperscript{108} The consultation may be rushed and conducted in a cramped environment rather than proceeding at a more relaxed pace in a customized environment. If a palliative care follow-up is required independent of an oncology appointment, this may be challenging to schedule because of space limitations. In large centers where oncology clinics are organized by tumor site, it may be unrealistic to have a physician or nurse in each clinic. Thus a model that relies exclusively on embedded practices may be unrealistic to have a physician or nurse in each clinic.\textsuperscript{17} It may be challenging to plan palliative care resources and manpower, as referrals may be unpredictable from day to day,\textsuperscript{100} with resources potentially spread across a variety of clinics.\textsuperscript{75} Because the principles of symptom management and ACP are universal across all tumor sites, the need to sub-specialize within individual oncology clinics is likely unwarranted. Finally, there is scant published literature regarding embedded clinics. One study reported poor recruitment (only 3 of 13 patients who were approached agreed to be seen by the palliative care consultant), primarily because of a lack of willingness to engage in an additional consultation or deteriorating health status.\textsuperscript{111}

In summary, the embedded clinic model may be the best available option for centers that are newly developing an outpatient clinic and allows for the promotion of a palliative care model within the oncology team. However, it is not optimal for larger centers where palliative care services are well established.

Nurse Practitioners and Nurse-Led Palliative Care
Nurses specialized in palliative care may enhance the level of palliative care delivery in the oncology setting. Advanced practice nurses or registered nurses may work as specialists embedded within oncology clinics or may be available by telephone or in person on an as-needed basis. As discussed above, RCTs on nurse-led palliative care have yielded mixed findings (Table 1).\textsuperscript{31,33–37} Other studies involving nurse-led models are hampered by limitations in study design that complicate their interpretation.\textsuperscript{112} In a nonrandomized study, the presence of a palliative care advanced practice nurse within a community cancer center was associated with lower rates of hospitalization (OR, 0.16; \(P < .01\)) and improved survival at 4 months (OR, 24.6; \(P = .02\)), but there was no improvement in quality of life or symptom management.\textsuperscript{113} Ferrell et al conducted a large study examining a nurse-led palliative care intervention in which patients with stage I through IV nonsmall cell lung cancer received an initial assessment followed by a discussion at an interdisciplinary team meeting and then nursing education over 4 sessions, and some improvements in quality of life were reported in a before-after comparison.\textsuperscript{71} Interestingly, the beneficial effect was observed mostly in patients with stage I through IIIB disease instead of those with stage IV disease, although the timing of inception for patient enrollment was not clearly defined. Walling et al embedded a palliative care nurse practitioner in 2 breast medical oncology clinics.\textsuperscript{114} Compared with 35 oncology clinics that did not have a nurse practitioner, there was greater referral for psychosocial support, ACP, and hospice referral. However, symptoms and quality-of-life outcomes were not assessed.

Nurse-led models may be less expensive to implement than interdisciplinary palliative care teams. They may increase the level of palliative care available at some oncology clinics while allowing for the mentoring of clinic nurses who provide oncology care.\textsuperscript{115} However, the billing and remuneration aspects of nurse-based models need further clarification.\textsuperscript{100} Similar to the embedded model, it may be difficult to ensure that each clinic is staffed with a palliative care nurse in larger centers. Because one discipline in isolation is unlikely
to allow patients and families to benefit from the attention to all aspects of quality of life, nurse-led palliative care should be regarded as complementary to (rather than replacing) interdisciplinary palliative care teams.

Palliative Care Delivered by Oncology Teams

There are limited data describing optimal models of primary palliative care provided by oncology teams alone. A pilot study was conducted using oncology clinic nurses trained in a care management intervention to facilitate symptom assessment, engage in ACP, provide emotional support to patients and caregivers, and communicate with other oncology team members. This model was feasible and acceptable to patients, families, and oncologists; a cluster RCT of this intervention is ongoing. Of note, care delivered by oncology teams alone was the control arm in several RCTs demonstrating improved quality of life when a palliative care team was also involved. In one of those trials, patients perceived clear differences in the focus (disease vs person/family), motive (managing cancer treatment vs managing symptoms), and model of care (physician-led, time-constrained vs patient-led, flexible) in oncology versus palliative care clinics. These findings underscore the complexity of palliative care and indicate that additional education of oncology clinicians is required to more comprehensively address palliative care needs.

This “solo practice” model of palliative care delivered by oncology teams has some advantages (Table 3). Patients benefit from the ability to access good symptom support from early in their diagnosis; many may not require secondary palliative care input and can benefit from completely integrated care from diagnosis to death. Oncology teams, in turn, may derive additional professional satisfaction from being able to provide symptom support, especially in areas where access to specialist palliative care teams may be limited.

Potential limitations to the provision of primary palliative care by oncology teams include the time required within oncology clinics to adequately address all aspects of care. Maintaining competencies in both active anticancer treatment modalities and symptom assessment and management may be challenging, if not impossible. For oncology teams without access to multidisciplinary support, fully holistic care may not be feasible, and the risk of burnout may be increased. The needs of caregivers may be overlooked in busy clinical settings, and psychosocial and bereavement support may be challenging to coordinate: palliative care teams may be better able to address these needs. Managing transitions in care, including the switch from active anticancer therapy to a purely supportive care approach, may be difficult to balance in a primary palliative care role. In addition, relationships with patients may be based upon expectations of maintaining positivity and hope, which may be impacted by attempts to direct care toward a purely symptom management approach.

Automatic Referral With Standardized Criteria

In the era of personalized cancer care, patients who have the greatest supportive care needs may be identified and automatically referred to specialist palliative care (Fig. 6C). This approach requires: 1) routine screening of supportive care needs; 2) predefined referral criteria with clinician endorsement; and 3) an automatic referral system in place. Importantly, this more targeted approach should not replace clinical judgement, but it can help to inform the treating oncologist to augment care.

Recent studies suggest that routine symptom assessment in the ambulatory oncology setting improves not only quality of life but also survival. The Commission on Cancer mandates routine distress screening, with the Distress Thermometer and the Edmonton Symptom Assessment System being used frequently. These efforts will likely result in greater awareness of symptom distress and timely, targeted referral.

Ongoing work is being conducted to identify proper standardized criteria, based on care needs and/or timing, to trigger referrals. Patients generally prefer to be referred based on their needs; one study found that those who felt palliative care referral was too early had limited symptom burden at the time of referral. Referral based on patient care needs also is supported by the findings from a 2016 international consensus panel. After 3 rounds of deliberation, a panel of 60 experts reached consensus on 11 major criteria for referral to outpatient palliative care. Patients who met any one of the criteria would be appropriate for referral. Interestingly, 9 of the 11 criteria were based on patient care needs, and only 2 were time-based (Table 4). Active work is underway to validate the use of these criteria to facilitate referral. In another population-based study of over 11,000 patients, the palliative performance scale (PPS) was used to assign patients as stable (PPS, 70%-100%), transitional (PPS, 40%-60%), end of life (PPS, 10%-30%), or dead. Entry into the transitional state (PPS, ≤60%) was considered a potential indicator for palliative care referral. Although a poor performance status may be a good trigger because it indicates greater functional need and shorter survival, the interrater reliability of performance status assessment is suboptimal. Patient completion of performance status tools is one option to overcome this, but patients’ self-rated scores tend to be worse than those of physicians.

The strengths and weakness of automatic referral models are highlighted in Table 3. In addition to streamlining referral and triaging resources, automatic referral can help to standardize care and normalize the process of referral. There are several challenges with automatic referral.
First, implementation of routine symptom screening in the oncology setting requires resources, commitment, and the identification of an appropriate questionnaire, along with cutoffs to trigger referral. Second, routine screening inevitably will result in false-negatives and positives, and procedures need to be established to address these issues. Third, the palliative care team needs to have adequate resources to handle the increased volume of referrals. Finally, the literature on automatic referral is still evolving, and only a few groups have published their experience.

In a quality-improvement project, the Edmonton Symptom Assessment System was used in a community hospital for distress screening in patients with cancer. Patients were assessed by a social worker for triaging if they screened positive, which was defined as at least 3 of 8 target symptoms with an intensity of 7 or greater on a scale of 10. Comparing between the 4-week periods before and after program implementation, there was a significant increase in social work assessments (21% vs 79%; \( P < .001 \)) and a nonstatistically significant trend toward increased palliative care referrals (12% vs 28%; \( P = .21 \)) among patients who screened positive. Other groups have also reported their preliminary experience related to distress screening to trigger supportive/palliative care referrals.

### Summary/Key Points

- There is strong evidence to support stand-alone palliative care clinics to improve patient outcomes. These clinics are ideally staffed with an interdisciplinary team in larger centers. These clinics represent the current standard of care against which other outpatient models should be measured.
- Embedded clinics may be more suitable in smaller centers with limited palliative care resources.
- Further research is needed to assess the impact of nurse-led palliative care and how this care model interfaces with specialist palliative care teams.
- RCTs have found that oncology teams delivering palliative care alone resulted in poorer quality-of-life outcomes versus concurrent care with a specialist palliative care team; however, it is important that all oncologists are trained in providing a basic level of palliative care.
- Automatic referral to palliative care may allow for more personalized care. It requires routine screening, standardized referral criteria, and an established palliative care team.
- An international consensus study identified 9 needs-based criteria and 2 time-based criteria for referral to outpatient palliative care for patients with advanced cancer.

### CONCLUSIONS

Patients with cancer have significant supportive/palliative care needs along their disease journey. These needs are growing because of an aging population with multiple comorbidities, increased numbers of patients living with advanced cancer for longer periods, greater emphasis on quality of life, and heightened awareness as a result of more widespread symptom screening. Specialist palliative care teams are well positioned to complement the primary palliative care provided by oncologists toward improving patients’ quality of life, symptom control, mood, end-of-life care, and satisfaction.

Evidence from RCTs supports the interdisciplinary nature of palliative care. Palliative care teams provide broad expertise to support the multidimensional care needs of patients and their caregivers. Timely palliative care further enables the team to provide longitudinal pharmacologic interventions, counseling, education, monitoring, and care planning to prevent crises, such as emergency room visits and intensive care unit admissions.

In the era of personalized medicine, the provision of palliative care should be tailored to provide the right level of intervention for the right patient in the right setting at the right time. By anticipating the natural history of advanced cancer and the potential challenges ahead, palliative care can proactively introduce multidimensional measures to improve quality of life throughout the disease course and ensure that end-of-life care is consistent with patients’ wishes. Many innovative care models are being considered to meet the increasing demand for palliative care services.

### TABLE 4. Major Criteria for Outpatient Palliative Care Referral Based on an International Consensus Panel

| CRITERIA                                      | CATEGORY                  |
|-----------------------------------------------|---------------------------|
| 1. Severe physical symptom(s)                 | Need-based criteria, distress |
| 2. Severe emotional symptom(s)                | Need-based criteria, distress |
| 3. Request for hastened death                 | Need-based criteria, distress |
| 4. Spiritual or existential crisis            | Need-based criteria, distress |
| 5. Assistance with decision making/ care planning | Need-based criteria, care needs |
| 6. Patient request                            | Need-based criteria, care needs |
| 7. Delirium                                   | Need-based criteria, neurologic |
| 8. Brain or leptomeningeal metastases         | Need-based criteria, neurologic |
| 9. Spinal cord compression or cauda equina    | Need-based criteria, neurologic |
| 10. Within 3 mo of diagnosis of advanced/incurable cancer for patients with a median survival ≤1 y | Time-based criteria |
| 11. Diagnosis of advanced cancer with progressive disease despite second-line systemic therapy (incurable) | Time-based criteria |

CTA: The Canadian Association of Clinical Biochemistry and the Canadian Society of Clinical Biochemists.
developed to foster improved integration between oncology and palliative care teams. There is strong evidence to support stand-alone palliative care clinics that provide interdisciplinary and timely care. Given the scarce palliative care resources, routine screening coupled with automatic referral may allow a more streamlined approach to identifying the patients most likely to benefit from palliative care, akin to the use of molecular testing for targeted therapies.

The provision of palliative care in the oncology clinic can be enhanced by: 1) increasing the delivery of primary palliative care by oncology teams; 2) introducing nurses/practitioners with specialized palliative care training; and/or 3) embedding palliative care physicians/specialists. These models may have an important role in rural areas and/or smaller community centers, but they do not replace the need for specialist interdisciplinary palliative care teams for patients with more complex needs. The evidence to support these models is still limited, and more research is needed to determine how palliative care can further integrate with oncology to personalize supportive care for each patient.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics. 2018. CA Cancer J Clin. 2018;68:7-30.

2. Portenoy RK, Thaler HT, Kornblith AB, et al. Symptom prevalence, characteristics and distress in a cancer population. Qual Life Res. 1994;3:183-189.

3. Chang VT, Hwang SS, Fireman M, Kasimis BS. Symptom and quality of life survey of medical oncology patients at a Veterans Affairs Medical Center: a role for symptom assessment. Cancer. 2000;88:1175-1183.

4. Whelan TJ, Mohide EA, Willan AR, et al. The supportive care needs of newly diagnosed cancer patients attending a regional cancer center. Cancer. 1997;80:1518-1524.

5. Fitzmaurice C, Dicker D, Pain A, et al. The global burden of cancer 2013. JAMA Oncol. 2015;1:505-527.

6. Cherny NI, Catane R; European Society of Medical Oncology Taskforce on Palliative and Supportive Care. Attitudes of medical oncologists toward palliative care for patients with advanced and incurable cancer: report on a survey by the European Society of Medical Oncology Taskforce on Palliative and Supportive Care. Cancer. 2003;98:2502-2510.

7. Hui D, Cerana MA, Park M, Hess K, Bruera E. Impact of oncologists’ attitudes toward end-of-life care on patients’ access to palliative care. Oncologist. 2016;21:1149-1155.

8. Bruera E, Hui D. Integrating supportive and palliative care in the trajectory of cancer: establishing goals and models of care. J Clin Oncol. 2010;28:4013-4017.

9. Hui D, Kim SH, Kwon JH, et al. Access to palliative care among patients treated at a comprehensive cancer center. Oncologist. 2012;17:1574-1580.

10. Schenker Y, Crowley-Matoka M, Dohan D, et al. Oncologist factors that influence referrals to subspecialty palliative care clinics. J Oncol Pract. 2013;10:e37-e44.

11. Hui D, Titus A, Curtis T, et al. Implementation of the Edmonton Symptom Assessment System for symptom distress screening at a community cancer center: a pilot program. Oncologist. 2017;22:995-1001.

12. Commission on Cancer, American College of Surgeons. Cancer Program Standards: Ensuring Patient-Centered Care. Chicago, IL: American College of Surgeons; 2016. fais.org/quality%20programs/cancer/coc/standards.

13. Hui D, Parsons HA, Damani S, et al. Quantity, design, and scope of the palliative oncology literature. Oncologist. 2011;16:694-703.

14. Jacobsen J, Jackson V, Dahlin C, et al. Components of early outpatient palliative care consultation in patients with metastatic nonsmall cell lung cancer. J Palliat Med. 2011;14:459-464.

15. Yoong J, Park ER, Greer JA, et al. Early palliative care in advanced lung cancer: a qualitative study. JAMA Intern Med. 2013;173:283-290.

16. Hannon B, Swami N, Pope A, et al. Early palliative care and its role in oncology: a qualitative study [published online ahead of print 2016]. Oncologist. pii: theoncologist.2016-0176.

17. Hui D, Bruera E. Integrating palliative care into the trajectory of cancer care. Nat Rev Clin Oncol. 2016;13:159-1571.

18. Greer JA, Jackson VA, Meier DE, Temel JS. Early integration of palliative care services with standard oncology care for patients with advanced cancer. CA Cancer J Clin. 2013;63:349-363.

19. Levy MH, Smith T, Alvarez-Perez A, et al. NCCN Clinical Practice Guidelines in Oncology. Palliative Care. Fort Washington, PA: National Comprehensive Cancer Network; 2017. nccn.org/professionals/physician_gls/default.aspx. Accessed April 19, 2017.

20. Ferrell BR, Temel JS, Temin S, et al. Integration of palliative care into standard oncology care: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol. 2017;35:96-112.

21. American Cancer Society. A Guide to Palliative or Supportive Care. Atlanta, GA: American Cancer Society; 2018. cancer.org/treatment/treatments-and-side-effects/palliative-care/supportive-care-guide.html. Accessed April 25, 2018.

22. World Health Organization. WHO Definition of Palliative Care. Geneva, Switzerland: World Health Organization; 2018. who.int/cancer/palliative/definition/en/. Accessed April 25, 2018.

23. Temel JS, Greer JA, Admane S, et al. Longitudinal perceptions of prognosis and goals of therapy in patients with metastatic non-small-cell lung cancer: results of a randomized study of early palliative care. J Clin Oncol. 2011;29:2319-2326.

24. Greer JA, Pirl WF, Jackson VA, et al. Effect of early palliative care on chemotherapy use and end-of-life care in patients with metastatic non-small-cell lung cancer. J Clin Oncol. 2012;30:394-400.

25. Zimmermann C, Swami N, Krzyzanowska M, et al. Early palliative care for patients with advanced cancer.
a cluster-randomised controlled trial. *Lancet*. 2014;383:1721-1730.

26. Temel JS, Greer JA, El-Jawahri A, et al. Effects of early integrated palliative care in patients with lung and GI cancer: a randomized clinical trial. *J Clin Oncol*. 2016;35:834-841.

27. El-Jawahri A, Greer JA, Pirl WF, et al. Effects of early integrated palliative care on caregivers of patients with lung and gastrointestinal cancer: a randomized clinical trial. *Oncologist*. 2017;22:1528-1534.

28. Maltoni M, Scarpi E, Dall’Agata M, et al. Systematic versus on-demand early palliative care: a randomised clinical trial assessing quality of care and treatment aggressiveness near the end of life. *Eur J Cancer*. 2016;65:61-68.

29. Groenvold M, Petersen MA, Damkier A, et al. Randomised clinical trial of early specialist palliative care plus standard care versus standard care alone in patients with advanced cancer: the Danish Palliative Care Trial. *Palliat Med*. 2017;31:814-824.

30. Bakitas M, Lyons KD, Hegel MT, et al. Effects of a palliative care intervention on clinical outcomes in patients with advanced cancer: the Project ENABLE II randomized controlled trial. *JAMA*. 2009;302:741-749.

31. Hui D, Bansal S, Strasser F, et al. Effectiveness of specialized palliative care: a systematic review. *BMJ*. 2017;6:CD011129.

32. Bakitas M, Tosteson T, Li Z, et al. Early versus delayed initiation of concurrent palliative oncology care: patient outcomes in the ENABLE III randomised controlled trial. *J Clin Oncol*. 2015;33:1438-1445.

33. Vanbutsele G, Pardon K, Van Belle S, et al. Effect of early and systematic integration of palliative care in patients with advanced cancer: a randomised controlled trial. *Lancet Oncol*. 2018;19:394-404.

34. Grudzen CR, Richardson LD, Johnson PN, et al. Emergency department-initiated palliative care in advanced cancer: a randomized clinical trial [published online ahead of print 2016]. *JAMA Oncol*. 2016. doi: 10/1001/jamaoncol.2015.5252.

35. Hearn J, Higginson IJ. Do specialist palliative care teams improve outcomes for cancer patients? A systematic literature review. *Palliat Med*. 1998;12:317-332.

36. Higginson IJ, Finlay I, Goodwin DM, et al. Do hospital-based palliative teams improve care for patients or families at the end of life? *J Pain Symptom Manage*. 2002;23:96-106.

37. Zimmermann C, Riegelmann R, Krzyzanowska M, Rodin G, Tannock I. Effectiveness of specialized palliative care: a systematic review. *JAMA*. 2008;299:1696-1709.

38. Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med*. 2010;363:733-742.

39. Kvaloieratos D, Corbeli J, Zhang D, et al. Association between palliative care and patient and caregiver outcomes: a systematic review and meta-analysis. *JAMA*. 2016;316:2104-2114.

40. Gaertner J, Siemens W, Meerpohl JJ, et al. Effect of specialist palliative care services on quality of life in adults with advanced incurable illness in hospital, hospice, or community settings: systematic review and meta-analysis [serial online]. *BMJ*. 2017;357:j2925.

41. Hui D, Bansal S, Strasser F, et al. Indicators of integration of oncology and palliative care programs: an international consensus. *Ann Oncol*. 2015;26:1953-1959.

42. Piril WF, Greer JA, Traeger L, et al. Depression and survival in metastatic non-small-cell lung cancer: effects of early palliative care. *J Clin Oncol*. 2012;30:1310-1315.
59. Hui D, Kim SH, Roquemore J, Dev R, Chisholm G, Bruera E. Impact of timing and setting of palliative care referral on quality of end-of-life care in cancer patients. *Cancer*. 2014;120:1743-1749.

60. Wright AA, Zhang B, Ray A, et al. Associations between end-of-life discussions, patient mental health, medical care near death, and caregiver bereavement adjustment. *JAMA*. 2008;300:1665-1673.

61. Phelps AC, Maciejewski PK, Nilsson M, et al. Religious coping and use of intensive life-prolonging care near death in patients with advanced cancer. *JAMA*. 2009;301:1140-1147.

62. Mack JW, Weeks JC, Wright AA, Block SD, Prigerson HG. End-of-life discussions, goal attainment, and distress at the end of life: predictors and outcomes of receipt of care consistent with preferences. *J Clin Oncol*. 2010;28:1203-1208.

63. Gomes B, Calanzani N, Curiale V, McCrone P, Higginson IJ. Effectiveness and cost-effectiveness of home palliative care services for adults with advanced illness and their caregivers [serial online]. *Cochrane Database Syst Rev*. 2013;6:CD007760.

64. Jang RW, Krzyzanowska MK, Zimmermann C, Taback N, Alibhai SM. Palliative care and the aggressiveness of end-of-life care in patients with advanced pancreatic cancer [serial online]. *J Natl Cancer Inst*. 2015;107:duj424.

65. Ziegler LE, Craigs CL, West RM, et al. Is palliative care support associated with better quality end-of-life care indicators for patients with advanced cancer? A retrospective cohort study [serial online]. *BMJ Open*. 2018;8:e018284.

66. Pellizzari M, Hui D, Pinato E, et al. Palliative care consultation in patients with advanced pancreatic cancer: a qualitative study of oncologists' approaches to end-of-life care. *J Palliat Med*. 2008;11:893-906.

67. Hui D, Park M, Liu D, Reddy A, Dalal S, Bruera E. Attitudes and beliefs toward supportive and palliative care referral among hematologic and solid tumor oncology specialists. *Oncolist*. 2015;20:1326-1332.

68. Buss MK, Lessen DS, Sullivan AM, Von Roenn J, Arnold RM, Block SD. Hematology/oncology fellows' training in palliative care: results of a national survey. *Cancer*. 2011;117:4304-1431.

69. Hui D, Elsayem A, De la Cruz M, et al. Availability and integration of palliative care at US cancer centers. *JAMA*. 2010;303:1054-1061.

70. Wong A, Hui D, Egner M, et al. Advanced cancer patients’ self-reported perception of timeliness of their referral to outpatient supportive/palliative care and their survival data [abstract]. *J Clin Oncol*. 2017;35(15 suppl):10121.

71. Ferrell B, Sun V, Hurria A, et al. Interdisciplinary palliative care for patients with lung cancer. *J Pain Symptom Manage*. 2015;50:758-767.

72. Wentlandt K, Krzyzanowska MK, Swami N, Rodin GM, Le LW, Zimmermann C. Referral practices of oncologists to specialized palliative care. *J Clin Oncol*. 2012;30:4380-4386.

73. Rangachari D, Smith TJ. Integrating palliative care in oncology: the oncologist as a primary palliative care provider. *Cancer J*. 2015;19:373-378.

74. vonGunten CF. Secondary and tertiary palliative care in US hospitals. *JAMA*. 2002;287:875-881.

75. Hui D, Bruera E. Models of integration of oncology and palliative care. *Ann Palliat Med*. 2015;4:89-98.

76. Quill TE, Abernethy AP. Generalist plus specialist palliative care—creating a more sustainable model. *N Engl J Med*. 2013;368:1173-1175.

77. Lupu D. Estimate of current hospice and palliative medicine physician workforce shortage. *J Pain Symptom Manage*. 2010;40:899-911.

78. Jackson VA, Mack J, Matsuyama R, et al. A qualitative study of oncologists' response to an outpatient palliative care consultation in patients with advanced cancer and cancer pain. *J Pain Symptom Manage*. 2012;44:340-350.

79. Wright AA, Zhang B, Keating NL, Weeks JC, Prigerson HG. Associations between palliative chemotherapy and adult cancer patients’ end of life care and place of death: prospective cohort study [serial online]. *BMJ* 2014;348:g1219.

80. Calton BA, Alvarez-Perez A, Portman DG, Ramchandran KJ, Sugalski J, Rabow MW. The current state of palliative care for patients cared for at leading US cancer centers: the 2015 NCCN Palliative Care Survey. *J Natl Compr Canc Netw*. 2016;14:859-866.

81. Fainsinger RL. Palliative care in Edmonton. *Support Care Cancer*. 1995;3:91-92.

82. Fainsinger RL, Brenneis C, Fassbender K. Edmonton, Canada: a regional model of palliative care development. *J Pain Symptom Manage*. 2007;33:634-639.

83. Hannon B, Swami N, Pope A, et al. The oncology palliative care clinic at the Princess Margaret Cancer Centre: an early intervention model for patients with advanced cancer. *Support Care Cancer*. 2015;23:1073-1080.

84. The Walsh D, Harry R, Horvitz Center for Palliative Medicine (1987–1999): development of a novel comprehensive integrated program. *Am J Hosp Palliat Care*. 2001;18:239–250.

85. Mazzocato C, Stiefel F, Ducret S, Vagnair A. Palliative care in the University Hospital Lausanne: from consultations to an integrated regional program. *Support Care Cancer*. 1999;7:221-223.
95. Smith AK, Thaï JN, Bakitas MA, et al. The diverse landscape of palliative care clinics. *J Palliat Med.* 2013;16:661-668.

96. Zimmermann C, Seccareccia D, Clarke A, Harr D, Rodin G. Bringing palliative care to a Canadian cancer center: the palliative care program at Princess Margaret Hospital. *Support Care Cancer.* 2006;14:982-987.

97. Dev R, Fabbro ED, Miles M, Vala A, Hui D, Bruera E. Growth of an academic palliative medicine program: patient encounters and clinical burden. *J Pain Symptom Manage.* 2013;45:261-271.

98. Dalal S, Bruera S, Hui D, Yenno S, Dev R, Williams J, et al. Use of palliative care services in a tertiary cancer center. *Oncologist.* 2016;21:110-118.

99. Strasser F, Sweeney C, Willey J, Benisch-Dalal S, Bruera S, Hui D, Yennu S, Devner A, Warr D, Rodin G. Bringing palliative care services in a tertiary cancer center: a half-day multidisciplinary symptom control and palliative care outpatient clinic in a comprehensive cancer center on recommendations, symptom intensity, and patient satisfaction: a retrospective descriptive study. *J Pain Symptom Manage.* 2004;27:481-491.

100. Meier DE, Beresford L. Outpatient clinics are a new frontier for palliative care. *J Palliat Med.* 2008;11:823-828.

101. McDonald J, Swami N, Hannon B, et al. Impact of early palliative care on caregivers of patients with advanced cancer: cluster randomised trial. *Ann Oncol.* 2017;28:163-168.

102. Perez-Cruz P, Nguyen L, Rhondali W, et al. Attitudes and perceptions of patients, caregivers, and health care providers toward background music in patient care areas: an exploratory study. *J Palliat Med.* 2012;15:1130-1136.

103. Pimentel LE, Yennurajalingam S, Chisholm G, et al. The frequency and factors associated with the use of a dedicated supportive care center telephone triaging program in patients with advanced cancer at a comprehensive cancer center. *J Pain Symptom Manage.* 2015;49:939-944.

104. Delgado-Guay MO, Kim YJ, Shin SH, et al. Avoidable and unavoidable visits to the emergency department among patients with advanced cancer receiving outpatient palliative care. *J Pain Symptom Manage.* 2015;49:497-504.

105. Muir JC, Daly F, Davis MS, et al. Integrating palliative care into the outpatient, private practice oncology setting. *J Pain Symptom Manage.* 2010;40:126-135.

106. Cassel JB, Webb-Wright J, Holmes J, Lyckholm L, Smith TJ. Clinical and financial impact of a palliative care program at a small rural hospital. *J Palliat Med.* 2010;13:1339-1343.

107. Einstein DJ, DeSanto-Madeya S, Gregas M, Lynch J, McDermott DF, Buss MK. Improving end-of-life care: palliative care embedded in an oncology clinic specializing in targeted and immune-based therapies. *J Oncol Pract.* 2017;13:e729-e737.

108. Schenker Y, Bahary N, Claxton R, et al. A pilot trial of early specialty palliative care for patients with advanced pancreatic cancer: challenges encountered and lessons learned. *J Palliat Med.* 2018;21:28-36.

109. Zimmermann C, Swami N, Krzyzanowska M, et al. Perceptions of palliative care among patients with advanced cancer and their caregivers. *Can Med Assoc J.* 2016;188:E217-E227.

110. Gidwani R, Nevedal A, Patel M, et al. The appropriate provision of primary versus specialist palliative care to cancer patients: oncologists’ perspectives. *J Palliat Med.* 2017;20:395-403.

111. Johnston B, Buchanan D, Papadopoulou C, Sandeman G, Lord H. Integrating palliative care in lung cancer: an early feasibility study. *Int J Palliat Nurs.* 2013;19:433-437.

112. Meisenberg BR, Graze L, Brady-Copertino CJ. A supportive care clinic for cancer patients embedded within an oncology practice. *J Community Support Oncol.* 2014;12:205-208.

113. Prince-Paul M, Burant CJ, Saltzman JN, Teston LJ, Matthews CR. The effects of integrating an advanced practice palliative care nurse in a community oncology center: a pilot study. *J Support Oncol.* 2010;8:21-27.

114. Walling AM, D’Ambrosuo SF, Malin JL, et al. Effect and efficiency of an embedded palliative care nurse practitioner in an oncology clinic. *J Oncol Pract.* 2017;13:e792-e799.

115. Tartaglione EV, Vig EK, Reinke LF. Bridging the cultural divide between oncology and palliative care subspecialties: clinicians’ perceptions on team integration. *Am J Hosp Palliat Care.* 2018;35:978-984.

116. Schenker Y, White D, Rosenzweig M, et al. Care management by oncology nurses to address palliative care needs: a pilot trial to assess feasibility, acceptability, and perceived effectiveness of the CONNECT intervention. *J Palliat Med.* 2015;18:232-240.

117. Becker CL, Arnold RM, Park SY, et al. A cluster randomized trial of a primary palliative care intervention (CONNECT) for patients with advanced cancer: protocol and key design considerations. *Contemp Clin Trials.* 2017;54:98-104.

118. Bakitas M, Lyons KD, Hегel MT, Ahles T. Oncologists’ perspectives on concurrent palliative care in a National Cancer Institute-designated comprehensive cancer center. *Palliat Support Care.* 2013;11:415-423.

119. Pfeil TA, Laryinova K, Reiter-Theil D, Hiddemann W, Winkler EC. What keeps oncologists from addressing palliative care early on with incurable cancer patients? An active stance seems key. *Oncoologist.* 2015;20:56-61.

120. Tanco K, Rhondali W, Perez-Cruz P, et al. Patient perception of physician compassion after a more optimistic vs a less optimistic message: a randomized clinical trial. *JAMA Oncol.* 2015;1:176-183.

121. Hui D, Mori M, Meng YC, et al. Automatic referral to standarized palliative care access: an international Delphi survey. *Support Care Cancer.* 2018;26:175-180.

122. Strasser F, Blum D, von Moos R, et al. The effect of real-time electronic monitoring of patient-reported symptoms and clinical syndromes in outpatient workflow of medical oncologists: E-MOSAIC, a multicenter cluster-randomized phase III study (SAKK 95/06). *Ann Oncol.* 2016;27:324-332.

123. Basch E, Deal AM, Dueck AC, et al. Overall survival results of a trial assessing patient-reported outcomes for symptom monitoring during routine cancer treatment. *JAMA.* 2017;318:197-198.

124. Basch E, Deal AM, Kris MG, et al. Symptom monitoring with patient-reported outcomes during routine cancer treatment: a randomized controlled trial. *J Clin Oncol.* 2016;34:557-565.

125. Lo SB, Ianniello L, Sharma M, Sarnacki D, Finn KT. Experience implementing distress screening using the National Comprehensive Cancer Network distress thermometer at an urban safety-net hospital. *Psychooncology.* 2016;25:1113-1115.

126. Dudgeon D, King S, Howell D, et al. Cancer Care Ontario’s experience with implementation of routine physical and psychological symptom distress screening. *Psychooncology.* 2012;21:357-364.
127. Sutradhar R, Seow H, Earle C, et al. Modeling the longitudinal transitions of performance status in cancer outpatients: time to discuss palliative care. *J Pain Symptom Manage*. 2013;45:726-734.

128. Zimmermann C, Burman D, Bandukwala S, et al. Nurse and physician inter-rater agreement of three performance status measures in palliative care outpatients. *Support Care Cancer*. 2010;18:609-616.

129. Popovic G, Harhara T, Pope A, et al. Patient-reported functional status in outpatients with advanced cancer: correlation with physician-reported scores and survival. *J Pain Symptom Manage*. 2018;55:1500-1508.

130. Watanabe S, Nekolaichuk C, Beaumont C, Mawani A. The Edmonton Symptom Assessment System—what do patients think? *Support Care Cancer*. 2009;176:675-683.

131. Berry DL. Patient-reported symptoms and quality of life integrated into clinical cancer care. *Semin Oncol Nurs*. 2011;27:203-210.

132. Glare PA, Semple D, Stabler SM, Saltz LB. Palliative care in the outpatient oncology setting: evaluation of a practical set of referral criteria. *J Oncol Pract*. 2011;7:366-370.

133. Funk R, Cisneros C, Williams RC, Kendall J, Hamann HA. What happens after distress screening? Patterns of supportive care service utilization among oncology patients identified through a systematic screening protocol. *Support Care Cancer*. 2016;24:2861-2868.