

Integration of Palliative Care Into Standard Oncology Care: American Society of Clinical Oncology Clinical Practice Guideline Update

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Editor's note: This American Society of Clinical Oncology clinical practice guideline provides recommendations, with comprehensive review and analyses of the relevant literature for each recommendation. Additional information, including a Data Supplement with additional evidence tables, a Methodology Supplement, slide sets, clinical tools and resources, and links to patient information at www.cancer.net, is available at www.asco.org/palliative-care-guideline and www.asco.org/guidelineswiki.

Authors' disclosures of potential conflicts of interest are found in the article online at www.jco.org. Author contributions are found at the end of this article.

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ABSTRACT

Purpose

To provide evidence-based recommendations to oncology clinicians, patients, family and friend caregivers, and palliative care specialists to update the 2012 American Society of Clinical Oncology (ASCO) provisional clinical opinion (PCO) on the integration of palliative care into standard oncology care for all patients diagnosed with cancer.

Methods

ASCO convened an Expert Panel of members of the ASCO Ad Hoc Palliative Care Expert Panel to develop an update. The 2012 PCO was based on a review of a randomized controlled trial (RCT) by the National Cancer Institute Physicians Data Query and additional trials. The panel conducted an updated systematic review seeking randomized clinical trials, systematic reviews, and meta-analyses, as well as secondary analyses of RCTs in the 2012 PCO, published from March 2010 to January 2016.

Results

The guideline update reflects changes in evidence since the previous guideline. Nine RCTs, one quasiexperimental trial, and five secondary analyses from RCTs in the 2012 PCO on providing palliative care services to patients with cancer and/or their caregivers, including family caregivers, were found to inform the update.

Recommendations

Inpatients and outpatients with advanced cancer should receive dedicated palliative care services, early in the disease course, concurrent with active treatment. Referral of patients to interdisciplinary palliative care teams is optimal, and services may complement existing programs. Providers may refer family and friend caregivers of patients with early or advanced cancer to palliative care services.

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INTRODUCTION

The purpose of this version of the American Society of Clinical Oncology (ASCO) guideline is to update the 2012 ASCO provisional clinical opinion (PCO)¹ on the integration of palliative care into standard oncology care and transition the content into a guideline. The 2012 PCO was based on a review of the 2010 study by Temel et al² conducted by the National Cancer Institute Physicians Data Query and additional randomized controlled trials (RCTs) chosen by ASCO, showing the benefits of early palliative care when added to usual oncology care. As in the 2012 PCO, this document uses the definition of palliative care

from the National Consensus Project³ (provided in Bottom Line Box). Patients with advanced cancer are defined as those with distant metastases, late-stage disease, cancer that is life limiting, and/or with prognosis of 6 to 24 months. This update includes nine RCTs, as well as one quasiexperimental study and five secondary publications from previously reviewed RCTs. It reviews and analyzes new and updated evidence on early palliative care, including evidence on patients in both inpatient and outpatient settings, components of and triggers for offering patients palliative care, palliative care services for family caregivers, and how oncology professionals and other clinicians can provide palliative care, in addition to palliative care specialists. In this guideline, a family caregiver

THE BOTTOM LINE

Integration of Palliative Care Into Standard Oncology Care: American Society of Clinical Oncology Clinical Practice Guideline Update**Guideline Question**

Should palliative care concurrent with oncology care be standard practice?

Target Population

Patients with advanced cancer and their caregivers

Target Audience

Oncology clinicians, patients, caregivers, and palliative care specialists

Methods

An Expert Panel was convened to update clinical practice guideline recommendations based on a systematic review of the medical literature.

Key Recommendation

Patients with advanced cancer, whether patient or outpatient, should receive dedicated palliative care services, early in the disease course, concurrent with active treatment. Referring patients to interdisciplinary palliative care teams is optimal, and services may complement existing programs. Providers may refer caregivers of patients with early or advanced cancer to palliative care services.

Specific Recommendations

Patients with advanced cancer should be referred to interdisciplinary palliative care teams (consultation) that provide inpatient and outpatient care early in the course of disease, alongside active treatment of their cancer (type: evidence based, benefits outweigh harms; evidence quality: intermediate; strength of recommendation: strong).

Palliative care for patients with advanced cancer should be delivered through interdisciplinary palliative care teams with consultation available in both outpatient and inpatient settings (type: evidence based, benefits outweigh harms; evidence quality: intermediate; strength of recommendation: moderate).

Patients with advanced cancer should receive palliative care services, which may include referral to a palliative care provider. Essential components of palliative care may include:

- Rapport and relationship building with patients and family caregivers
- Symptom, distress, and functional status management (eg, pain, dyspnea, fatigue, sleep disturbance, mood, nausea, or constipation)
- Exploration of understanding and education about illness and prognosis
- Clarification of treatment goals
- Assessment and support of coping needs (eg, provision of dignity therapy)
- Assistance with medical decision making
- Coordination with other care providers
- Provision of referrals to other care providers as indicated

For newly diagnosed patients with advanced cancer, the Expert Panel suggests early palliative care involvement within 8 weeks of diagnosis (type: informal consensus, benefits outweigh harms; evidence quality: intermediate; strength of recommendation: moderate).

Among patients with cancer with high symptom burden and/or unmet physical or psychosocial needs, outpatient cancer care programs should provide and use dedicated resources (palliative care clinicians) to deliver palliative care services to complement existing program tools (type: evidence based, benefits outweigh harms; evidence quality: intermediate; strength of recommendation: moderate).

For patients with early or advanced cancer for whom family caregivers will provide care in the outpatient setting, nurses, social workers, or other providers may initiate caregiver-tailored palliative care support, which could include telephone coaching, education, referrals, and face-to-face meetings. For family caregivers who may live in rural areas and/or are unable to travel to clinic and/or longer distances, telephone support may be offered (type: evidence based; evidence quality: low; strength of recommendation: weak).

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THE BOTTOM LINE (CONTINUED)

Qualifying Statement

This guideline uses the National Consensus Project definition of palliative care: “Palliative care means patient and family-centered care that optimizes quality of life by anticipating, preventing, and treating suffering. Palliative care throughout the continuum of illness involves addressing physical, intellectual, emotional, social, and spiritual needs and to facilitate patient autonomy, access to information, and choice.”^{3(p9)}

ASCO believes that cancer clinical trials are vital to inform medical decisions and improve cancer care and that all patients should have the opportunity to participate. Patients in clinical trials may benefit from the support of palliative care.

Additional Resources

More information, including a Data Supplement with additional evidence tables, a Methodology Supplement with information about evidence quality and strength of recommendations, slide sets, and clinical tools and resources, is available at www.asco.org/palliative-care-guideline and www.asco.org/guidelineswiki. Patient information is available at www.cancer.net.

is defined as either a friend or a relative whom the patient describes as the primary caregiver; it may be someone who is not biologically related.⁴ The guideline also presents discussions on health disparities and on the business case for palliative care. This update complements discussions on palliative care in recent ASCO guidelines on the treatment of patients with stage IV non–small-cell lung cancer (NSCLC)⁵ and the treatment of patients with pancreatic cancer.^{6–8} We also suggest readers refer to the ASCO suite of supportive care guidelines (at <http://www.asco.org/practice-guidelines/quality-guidelines/guidelines/supportive-care-and-treatment-related-issues>) as well as the recently published ASCO chronic pain guideline.⁹

GUIDELINE QUESTIONS

This clinical practice guideline addresses six overarching clinical questions: What is the most effective way to care for patients with advanced-cancer symptoms? What are the most practical models of palliative care? How is palliative care in oncology defined or conceptualized? How can palliative care services relate in practice to other existing or emerging services? Which interventions are helpful for family caregivers (as described in Introduction)? Which patients should be offered or referred to palliative care services, and when in their disease trajectory; are there triggers that should be used to prompt specialty palliative care referrals?

METHODS

Guideline Update Development Process

The Expert Panel met via teleconference and Webinar and corresponded through e-mail (Appendix Table A1, online only). On the basis of the consideration of the evidence, the authors were asked to contribute to the development of the guideline, provide critical review, and finalize the guideline recommendations. Members of the Expert Panel were responsible for reviewing and approving the penultimate version of the guideline, which was then circulated for external review and submitted to *Journal of Clinical Oncology* for editorial review and consideration for publication. All ASCO guidelines are ultimately reviewed and approved by the Expert Panel and the ASCO Clinical Practice Guideline Committee before publication.

The recommendations were developed by an Expert Panel with multidisciplinary representation. ASCO guidelines staff supplemented and updated the literature search that was conducted to inform its recommendations on palliative care. PubMed was searched from March 2010 to January 2016. The panel based its recommendations on phase III RCTs, secondary analyses of RCTs discussed in 2012, and clinical experience. In some selected cases where evidence was lacking, but there was a high level of agreement among Expert Panel members, informal consensus was used (as noted with the Recommendations). Articles were selected for inclusion in the systematic review of the evidence based on the following criteria: the population discussed in the articles was patients diagnosed with cancer, and articles were fully published English-language reports of phase III RCTs or published secondary analyses of RCTs in the 2012 PCO, rigorously conducted systematic reviews, or meta-analyses.

Articles were excluded from the systematic review if they were: meeting abstracts not subsequently published in peer-reviewed journals; editorials, commentaries, letters, news articles, case reports, or narrative reviews; or published in a non-English language. The guideline recommendations were crafted, in part, using the Guidelines Into Decision Support (GLIDES) methodology and accompanying BRIDGE-Wiz software.¹⁰ Ratings for the type and strength of recommendation, evidence, and potential bias are provided with each recommendation (Methodology Supplement).

Detailed information about the methods used to develop this guideline update is available in the Methodology Supplement at www.asco.org/palliative-care-guideline, including an overview (eg, panel composition, development process, and revision dates), literature search and data extraction results, recommendation development process (GLIDES and BRIDGE-Wiz), and quality assessment.

The ASCO Expert Panel and guidelines staff will work with panel co-chairs to keep abreast of any substantive updates to the guideline. On the basis of a formal review of the emerging literature, ASCO will determine the need to update.

This is the most recent information as of the publication date. Visit the ASCO Guidelines Wiki at www.asco.org/guidelineswiki to submit new evidence.

Guideline Disclaimer

The clinical practice guidelines and other guidance published herein are provided by the American Society of Clinical Oncology, Inc. (ASCO) to assist providers in clinical decision making. The information herein should not be relied upon as being complete or accurate, nor should it be considered as inclusive of all proper treatments or methods of care or as a statement of the standard of care. With the rapid development of scientific knowledge, new evidence may emerge between the time information is developed and

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Guideline and Conflicts of Interest

The Expert Panel was assembled in accordance with the ASCO Conflict of Interest Policy Implementation for Clinical Practice Guidelines (“Policy,” found at <http://www.asco.org/rwc>). All members of the Expert Panel completed ASCO’s disclosure form, which requires disclosure of financial and other interests, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial impact as a result of promulgation of the guideline. Categories for disclosure include employment; leadership; stock or other ownership; honoraria; consulting or advisory role; speaker’s bureau; research funding; patents, royalties, other intellectual property; expert testimony; travel, accommodations, expenses; and other relationships. In accordance with the Policy, the majority of the members of the Expert Panel did not disclose any relationships constituting a conflict under the Policy.

RESULTS

A total of nine new RCTs,¹¹⁻¹⁹ two publications reporting on one large quasiexperimental trial,^{4,20} and five secondary publications based on prior published RCTs²¹⁻²⁵ met eligibility criteria and/or were suggested by the Expert Panel and form the evidentiary basis for the guideline recommendations. The identified trials were published between 2011 and 2016; three were specifically on family caregivers.^{4,13,17} The studies included patients with advanced or metastatic disease; the Ferrell et al²⁰ study also included patients with early-stage NSCLC. The Higginson et al¹⁵ trial included patients with lung cancer who had refractory breathlessness, as well as patients with diseases other than cancer, as the main criteria for entry. One study compared early with delayed palliative care.^{11,13} All of the studies included nurses in the intervention, and five included palliative care specialists.^{4,11,15,16,19,20} All of the studies included outpatients. The trial by Grudzen et al¹⁶ identified patients with cancer presenting to the emergency department, who were subsequently randomly assigned, and provided inpatient palliative care services. In addition, palliative care services were provided to patients enrolled in the clinical trial by Zimmermann et al¹⁹ and the previously reviewed Temel et al² study when they became inpatients. The authors emphasize that the evidence supporting this guideline is from patients with advanced cancers. There are emerging data on the potential benefits of palliative care to patients

with earlier-stage disease; however, more data are needed to consider a strong, evidence-based recommendation.

The primary outcomes for the studies included quality of life (QOL), symptom relief, psychological outcomes, survival, and satisfaction. The primary outcome for five of the trials for Clinical Question 1 was QOL,^{11,15,16,19,20} as it was in three of the trials for Clinical Questions 4, 5, and 6.^{4,13,18} In two of the studies relevant to Clinical Question 5, the primary outcomes included psychological distress and well-being or mood, although they were framed in a variety of ways,^{13,17} as they were for two studies informing Clinical Question 1.^{11,20} One study with these outcomes informed Clinical Questions 3 and 4.¹² Several studies had more than one primary outcome.

Table 1 lists the RCTs that were particularly pertinent to the development of the recommendations (characteristics of secondary analyses are included in the Data Supplement). The identified trials were published between 2011 and 2016 (characteristics of the participants in the studies are listed in the Data Supplement).

Study quality was formally assessed for the nine RCTs and one quasiexperimental study identified (Table 2). An assessment of study quality was performed for included evidence by one methodologist. Study design aspects related to individual study quality, such as randomization method and allocation concealment, and risk of bias were evaluated. The assessment generally indicated low potential risk of bias for most of the identified evidence. Refer to the Methodology Supplement for definitions of ratings for overall potential risk of bias and the Data Supplement for ratings of individual studies and assessment instruments for QoL measurement (studies used).

FINAL RECOMMENDATIONS

CLINICAL QUESTION 1

What is the most effective way to care for patients with advanced-cancer symptoms (palliative care services in addition to usual care compared with usual care alone)?

Recommendation 1

Patients with advanced cancer should be referred to interdisciplinary palliative care teams (consultation) that provide inpatient and outpatient care early in the course of disease, alongside active treatment of their cancer (type: evidence based, benefits outweigh harms; evidence quality: intermediate; strength of recommendation: strong).

Literature review update and analysis. Trials that serve as the foundation for much of the research described in this update include the Temel et al² study and the ENABLE (Educate, Nurture, Advise Before Life Ends) II study,²⁶ both described in the 2012 PCO.¹ Briefly, the Temel et al phase III RCT in patients with newly diagnosed NSCLC compared early palliative care with standard care in an outpatient setting. Patients in the intervention arm had higher QOL, less aggressive end-of-life (EOL) care, lower rates of depression, and longer survival of 2.7 months. The ENABLE II study randomly assigned patients with advanced cancer to an advanced practice nursing palliative care intervention versus usual care and found higher QOL and lower depressed mood with the intervention. Subsequent studies by these investigators and others attempted to tease out which elements of palliative care contributed to the positive results. The

Table 1. Study Characteristics

| Reference | Study Design | Study Population | Cancer Type | Study Arm | | | Sample Size Analyzed | Study Duration | |
|---------------------------|---|---|--|--|--|------------------------------------|---|-------------------------------------|--|
| | | | | 1: PC Intervention | 2: Comparator or Control | 3: Intervention | | | |
| Bakitas ¹¹ | Fast-track RCT | Patients with advanced cancer at NCI cancer centers, VA medical centers, and community outreach clinics | Advanced-stage solid tumor or hematologic malignancy | Early initiation of palliative care (within 30 to 60 days postdiagnosis) | Delayed initiation of palliative care (3 months postdiagnosis) | NA | Early, n = 104 | Delayed, n = 103 | October 2010 to March 2013 |
| Chochinov ¹² | RCT | Patients (age ≥ 18 years) with terminal prognosis (life expectancy ≤ 6 months) | Lung, breast, GI, GU, gynecologic, hematologic, brain, or other cancer | Dignity therapy | Standard palliative care | Client-centered care | 108 | Arm 2, n = 111; arm 3, n = 107 | April 2005 to October 2008 |
| Dionne-Odom ¹³ | RCT | Caregivers of patients with advanced cancer | Advanced-stage solid tumor or hematologic malignancy | Early initiation of palliative care (within 30 to 60 days postdiagnosis) | Delayed initiation of palliative care (3 months postdiagnosis) | NA | Caregivers early, n = 61 | Caregivers delayed, n = 61 | October 2010 to March 2013 |
| Dyar ¹⁴ | Randomized pilot study | Patients with metastatic cancer | Breast, lung, prostate, or other cancer | ARNP-directed intervention | Standard care | NA | 12 | 14 | Accrual: November 13, 2008, to July 28, 2009 |
| Ferrell ²⁰ | Prospective, quasiexperimental study | Patients with stage I to IV NSCLC | NSCLC | Interdisciplinary palliative care intervention | Usual care | Usual care | 272 (early-stage disease, n = 130; late-stage disease, n = 142) | 219 (early, n = 105; late, n = 114) | Primary outcome analysis: 12 weeks |
| Grudzen ¹⁶ | RCT | Patients with advanced cancer presenting to emergency department | Breast, CRC, lung, or other cancer | Palliative care intervention | Standard care | Standard care | 69 | 67 | 12 weeks Recruitment: 12 weeks (June 2011 to April 2014) 6-week intervention |
| Higginson ¹⁵ | Single-blind randomized trial | Adults with refractory breathlessness and advanced disease (not 100% cancer)* | Multiple, primarily lung cancer | Breathlessness support service | Usual pulmonologist specialty care | Usual pulmonologist specialty care | 53 | 52 | |
| Hudson ¹⁷ | RCT | Primary family caregivers of patients with advanced cancer receiving home-based palliative care | Patients with stage I to IV NSCLC | One face-to-face visit | Standard care | Standard care | One visit, n = 57; two visits, n = 93 | 148 | |
| Sun ⁴ | Two-group, prospective, sequential, quasiexperimental study | Family caregivers | Patients with stage I to IV NSCLC | Presented at interdisciplinary care meetings, four educational sessions (organized in physical, psychological, social, and spiritual domains), self-care plans | Usual care | Usual care | 197 (191 pairs) | 157 (153 pairs) | July 2011 to August 2014 |

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Table 1. Study Characteristics (continued)

| Reference | Study Design | Study Population | Cancer Type | Study Arm | | | Sample Size Analyzed | | Study Duration |
|--------------------------|--------------|--|---|------------------------------------|---|-----------------|----------------------|------------|---|
| | | | | 1: PC Intervention | 2: Comparator or Control | 3: Intervention | Palliative Care | Usual Care | |
| Uitdehaag ¹⁸ | RCT | Consecutive patients with unresectable or recurrent upper GI cancer | Upper GI cancer | Nurse-led follow-up at home | Conventional medical follow-up in outpatient clinic | NA | 36 | 30 | ≤ 13 months |
| Zimmermann ¹⁹ | Cluster RCT | Patients with stage IV or III cancer with poor clinical prognosis and estimated survival of 6 to 24 months | Lung, GI, GU, breast, or gynecologic cancer | Early palliative care intervention | Standard care | NA | 228 | 233 | 4 months (recruitment over 3.8 years: December 1, 2006, to February 28, 2011) |

Abbreviations: ARNP, advanced registered nurse practitioner; CRC, colorectal; GU, genitourinary; NA, not applicable; NCI, National Cancer Institute; NSCLC, non-small-cell lung cancer; RCT, randomized clinical trial; VA, Veterans Administration.

*—Participants were identified from respiratory medicine (50 [48%]), palliative care services (23 [22%]), general practices (15 [14%]), physiotherapy services (13 [12%]), and heart failure services [4%].^{16, p882}

Table 2. Study Quality Assessment

| Reference | Adequate Randomization | Concealed Allocation | Sufficient Sample Size | Similar Groups | Blinded | Validated and Reliable Measures | Adequate Follow-Up | Insignificant COIs | Overall Potential Risk of Bias* |
|---------------------------|------------------------|----------------------|---|--|------------------------|---------------------------------|--------------------------|--------------------|---------------------------------|
| Bakitas ¹¹ | √ | √ | — (did not meet target because of slow accrual) | Partial | Partial (not patients) | √ | √ | √ | Low |
| Chochinov ¹² | √ | √ | √ | √ | — | √ | √ | √ | Low |
| Dionne-Odom ¹³ | √ | √ | — (see Bakitas) | Partial | Partial | √ | √ | √ | Low |
| Dyar ¹⁴ | ? | ? | — | √ | — | √ | — (by report of authors) | √ | Intermediate |
| Ferrell ²⁰ | NA | NA | √ | — | — | √ | √ | √ | Intermediate? |
| Grudzen ¹⁶ | √ | — | ? | √ | Partial | √ | √ | √ | Low |
| Higginson ¹⁵ | √ | Partial | √ | √ | Partial | √ | ? | √ | High |
| Hudson ¹⁷ | √ | √ | √ | √ | Partial | √? | ? (shorter than others) | √ | Low? |
| Sun ⁴ | — | NR | ? | Partial | NR | √ | √ (comparable to others) | √ | ? |
| Uitdehaag ¹⁸ | √ | √ | — (below target) | √ | — | √ | √ (longer than most) | √ | Intermediate to high |
| Zimmermann ¹⁹ | √ | √ | √ | √ (with exception of prevalence of GU cancers) | — | √ | √ | √ | Low |

NOTE. Study quality was formally assessed for nine RCTs and one quasiexperimental study identified. Assessment of study quality was performed for included evidence by one methodologist. Study design aspects related to individual study quality (eg, randomization method and allocation concealment) and risk of bias were evaluated. Assessment generally indicated low potential risk of bias for most identified evidence. Methodology Supplement provides definitions of ratings for overall potential risk of bias; Data Supplement provides ratings of individual studies. √ indicates criteria were met; — indicates criteria were not met; ? indicates insufficient detail, not reported, and/or uncertain if criteria were met.
Abbreviations: COI, conflict of interest; GU, genitourinary; NA, not applicable; NR, not reported.
*Ratings are based on estimation of whether criterion was met and extent of potential bias, not simply on reporting.

studies that this guideline discusses were published after the 2012 PCO and build on the evidence it reviewed.

Zimmermann et al¹⁹ performed a cluster randomized trial of medical oncology clinics with 461 patients with stage IV or III solid tumors with clinical prognoses of 6 to 24 months, comparing standard care versus early palliative care in a free-standing palliative care clinic within a cancer center. The 4-month intervention included multidisciplinary assessment in a palliative care clinic, routine telephone and outpatient contacts, and an on-call service provided by palliative care clinicians. The primary outcome was change in QOL (Functional Assessment of Chronic Illness Therapy–Spiritual Well-Being [FACIT-Sp]) at 3 months. The study also measured other QOL outcomes and satisfaction with care. At 3 months, there was a nonsignificant trend toward a difference in FACIT-Sp (see Table 4 in the Data Supplement), whereas improvements in the Quality of Life at the End of Life (QUAL-E) QOL outcome and patient satisfaction were statistically significant. At 4 months, almost all measures favored the intervention with statistical significance, including FACIT-Sp and symptom intensity (which was not statistically significantly different at 3 months) measures. Strengths of the study included its power and the inclusion of patients with multiple types of cancer, widening the evidence base beyond patients with lung cancer. Limitations included the setting in a single cancer center and selection bias resulting from cluster randomization, which favored the standard care group.¹⁹

Another study found in the systematic review, by Dyar et al,¹⁴ compared a nurse practitioner–directed palliative care intervention versus usual care for patients with metastatic solid tumors. This was a

pilot study of 26 participants, and hospice referral was the primary outcome. The study was closed early after the publication of ENABLE II.²⁶ One QOL score improved with intervention (statistically significant; change from baseline mental QOL), as did the Functional Assessment of Cancer Therapy–General Measure (FACT-G) emotional score. As a result of several factors, such as follow-up and sample size, the investigators found it hard to assess the primary outcome. The primary limitation was small sample size.

Since the 2012 PCO,¹ other studies have involved participants with NSCLC (as did the 2010 Temel et al² study). Ferrell et al²⁰ performed a prospective, sequential, quasiexperimental study with 491 participants. The usual care group was recruited first, followed by recruitment of an intervention group. The intervention included baseline assessment, palliative care plan, interdisciplinary care meetings, palliative and/or supportive care referrals, and education sessions. The primary outcomes were QOL, symptom relief, and psychological distress at 12 weeks, with no specified primary outcome. The Ferrell et al study included patients with stage I to IV NSCLC (patients with early-stage NSCLC were not included in earlier trials). Stage differences were analyzed (early v late). QOL measures (FACT-Lung [FACT-L], Lung Cancer Subscale, Trial Outcome Index, spiritual well-being and psychological distress, FACIT-Sp, and Distress Thermometer) showed statistically significant differences favoring the palliative care group. Intervention participants received significantly more referrals, including to social work, chaplaincy, nutrition, and pain services, and more advanced EOL planning (all four measures). There were no statistically significant

differences in hospice use, EOL chemotherapy use, or survival. One strength of this study was its inclusion of participants with early-stage disease. A multivariable analysis found that patients with early-stage NSCLC had significantly higher QOL outcomes than those with late-stage disease. A limitation was that the study was a sequential trial, not an RCT, leading to possible selection bias.

The ENABLE III study by Bakitas et al¹¹ compared early versus delayed palliative care in 207 patients with new, progressive, or relapsed solid tumors or hematologic malignancies with prognoses of 6 to 24 months. The intervention included an in-person palliative care consultation, nurse-led telephone coaching sessions, and follow-up. Outcomes included QOL, 1-year survival, and resource use; no primary outcome was selected. As mentioned, the 2012 PCO¹ discussed the ENABLE II study. In ENABLE III, 4.8% of patients had hematologic malignancies, a group not included in many palliative care studies. Approximately 60% of the participants lived in rural areas. One-year survival was significantly improved ($P = .04$), although overall survival was not. The authors noted that regional palliative care quality improvement projects and growing acceptance of early palliative care as a standard of care may have affected recruitment and reduced the ability to reach the accrual target. In addition, half of the patients in the delayed group received palliative care consults earlier than specified in the protocol.

Grudzen et al¹⁶ randomly assigned 136 patients with cancer presenting to the emergency department at an academic urban center to usual care versus usual care plus a palliative care consultation that included symptom, spiritual, social need, and goals-of-care assessments. QOL, the primary outcome, was substantially improved. Median survival increased from 132 to 289 days, but this was not statistically significant. Health care use was not changed, and hospice use remained low, at 25% for both groups.

Higginson et al¹⁵ at Kings College London randomly assigned 105 patients with refractory breathlessness (of whom 20% had cancer) to usual pulmonologist specialty care versus the same plus a palliative care intervention. The intervention included a palliative care team, home physical therapy visits to teach energy conservation, a hand-held fan, and use of a poem as a mantra to help breathing and relaxation during crises. The main end point, the mastery domain of the Chronic Respiratory Disease Questionnaire, was significantly improved in the palliative care group, with a 16% improvement in breathlessness. The 6-week mean cost was £14 greater in the breathlessness support service group than the control group, despite the cost of the intervention. The same intervention was applied to 67 participants with advanced cancer who were referred to the breathless service (100%), either at presentation or after a 2-week delay, in a separate and smaller trial.²⁷ The service was judged effective, because breathlessness decreased by 1.29 (adjusted difference: 95% CI, -2.57 to -0.05 ; $P = .05$; scale, 0 to 10) and helpful; 68% of participants reported a significant impact in qualitative analyses. The service was judged cost effective, with total cost (including informal care) £354 less for the intervention group, combined with a small improvement in quality-adjusted life-years.

Greer et al²² reported on secondary outcomes of chemotherapy and hospice use in the 151 patients in the Temel et al² study. The outcomes of the secondary analysis included the total number of chemotherapy regimens for all participants, timing of chemotherapy administration, and hospice enrollment at EOL. Chemotherapy use at EOL was an exploratory outcome, not the primary outcome.

There was no difference in overall number of chemotherapy regimens. However, participants receiving early palliative care had lower chemotherapy use at EOL, with half the odds of receiving chemotherapy within 60 days of death (52.5% v 70.1%; $P = .05$; adjusted odds ratio, 0.47; 95% CI, 0.23 to 0.99; $P = .05$). There was also lower use of intravenous chemotherapy, but not of oral chemotherapy, during the last 60 days of life.

Another secondary analysis of the study by Temel et al² showed prognostic awareness is important and influences the care patients receive; just 9% of the patients in the palliative care plus usual care group received intravenous chemotherapy near EOL, versus 50% of those in the usual care group. Fourth- and fifth-line chemotherapy treatments have no proven benefit; however, they have the same adverse effects as earlier-line chemotherapy.^{28,29} There were similar rates of hospice referral in the two arms; intervention participants had earlier referrals for hospice services and longer stays than control participants. Limitations of these analyses included non-generalizability of benefits to other clinicians and patients, because the analyses were performed at an academic center with only patients with lung cancer.²²

Clinical interpretation. The review presented evidence supplementary to that reported in the ASCO PCO¹ and supports the integration of interdisciplinary palliative care services into the routine care of patients with advanced cancer. There is now robust evidence from multiple large clinical trials that early palliative care improves QOL, reduces depression, and improves satisfaction with care.^{2,11,19} Early palliative care also reduced the use of chemotherapy near EOL for patients with lung cancer and increased enrollment and length of stay in hospice,²² while improving survival.² In the quasiexperimental study in patients with lung cancer, benefits were noted primarily for patients with stage I to IIIB disease rather than stage IV disease.²⁰ Although the ENABLE III trial did not demonstrate a benefit in patient-reported outcomes, the study had limited power, and a substantial proportion of patients in the delayed group received palliative care early.¹¹ It is noteworthy that there were no adverse outcomes reported from early palliative care involvement in any of the trials.

CLINICAL QUESTION 2

What are the most practical models of palliative care? Who should deliver palliative care (external consultation, internal consultations with palliative care practitioners in the oncology practice, or performed by the oncologist him- or herself)?

Recommendation 2

Palliative care for patients with advanced cancer should be delivered through interdisciplinary palliative care teams, with consultation available in both outpatient and inpatient settings (type: evidence based, benefits outweigh harms; evidence quality: intermediate; strength of recommendation: moderate).

Literature review update and analysis. Literature relevant to this recommendation includes the Bakitas et al,¹¹ Ferrell et al,²⁰ Grudzen et al,¹⁶ Higginson et al,¹⁵ and Zimmermann et al¹⁹ studies described under Recommendation 1. There were no comparative health services delivery studies found, reflecting that alternative palliative care delivery has not been well studied. All the studies found were palliative care interventions (variable components) versus standard oncology care or early palliative care versus delayed

palliative care. Studies have demonstrated the value of outpatient multidisciplinary teams and telephone-based specialized palliative care interventions alongside standard care by the oncology team. Whether improved outcomes can be achieved through changes in health care delivery and training by oncology care providers has not been studied.

Clinical interpretation. Although palliative care delivery models for oncology patients are varied, the unifying elements among successful models include a palliative care provision by an interdisciplinary team available as a consultation service, with a presence in the outpatient as well as inpatient setting. In the primary studies, the providers were usually palliative care physicians (and advanced practice providers in some models) and/or palliative care nurses, at minimum.^{2,11,19} Some of the teams in the studies also included a social worker, chaplain, and/or rehabilitation specialist (physical therapy, occupational therapy, or rehabilitation medicine). Successful palliative care consultations provide comprehensive baseline and ongoing assessments that include evaluation of QOL and physical, psychological, spiritual, and social domains and prognostic disclosure (Appendix Table A2, online only).³⁰ A majority of successful palliative care models demonstrated in the literature operate as integrated consultants within the oncology clinic, which may enhance communication with oncology providers. Everyone who is involved with the care of patients and caregivers should be aware of the structure and importance of palliative care and have general knowledge and skill in palliative care practices.

Although most palliative care studies focus on referral of patients with advanced malignancy, one study discussed here, by Zimmermann et al,¹⁹ included patients with all stages of NSCLC and demonstrated that patients with earlier-stage disease received greatest benefit; however, further study is needed on this population.²⁰ The potential impact of palliative care interventions for patients with multiple types of earlier-stage cancer requires further study.

Oncologists may note that they are providing palliative care themselves. The palliative care studies have all use standardized symptom, spiritual, and psychosocial assessments, with an emphasis on early discussion of prognosis and treatment options to discern prognostic awareness and early discussion of hospice. On the basis of the current literature, it seems that the most practical means of providing the demonstrated benefits of palliative care for oncology patients is through a multidisciplinary palliative care team. It is possible that the beneficial elements of palliative care could also be provided by the primary oncology team. However, to achieve similar results in practice, clinicians should use the structured approach described in the studies. If this model is considered impractical because of workforce issues or other resource constraints, it is important to ensure that the important elements of palliative care discussed under Clinical Question 3 can be provided.

CLINICAL QUESTION 3

How is palliative care in oncology defined or conceptualized?

Recommendation 3

Patients with advanced cancer should receive palliative care services, which may include a referral to a palliative care provider. Essential components of palliative care include: rapport and relationship building with patient and family caregivers; symptom, distress, and

functional status management (eg, pain, dyspnea, fatigue, sleep disturbance, mood, nausea, or constipation); exploration of understanding and education about illness and prognosis; clarification of treatment goals; assessment and support of coping needs (eg, provision of dignity therapy); assistance with medical decision making; coordination with other care providers; and provision of referrals to other care providers as indicated. For newly diagnosed patients with advanced cancer, the Expert Panel suggests early palliative care involvement, starting early in the diagnosis process and ideally within 8 weeks of diagnosis (type: informal consensus; evidence quality: intermediate; strength of recommendation: moderate).

Literature review update and analysis. All of the palliative care intervention arms in the trials underwent standardized symptom, psychosocial, and spiritual assessments, although the exact instruments varied (Data Supplement). The goal of providing palliative care within 8 weeks is based on the 2010 Temel et al² report in which patients in the palliative care arm received palliative care within 8 weeks of diagnosis of metastatic disease (Clinical Question 6). The Jacobsen et al²³ secondary analysis of the Temel et al study involved only those in the intervention arm of the primary RCT; 67 of those participants were analyzed. Outcomes measured included health-related QOL (HRQOL) and mood, as well as time clinicians spent with patients and the elements of consultation. When patients' QOL and mood were lower, clinicians spent more time with them. A majority of the visits occurring soon after diagnosis and intervention were mainly devoted to symptom management (median time, 20 of 55 minutes on symptom management, 10 of 55 minutes on illness understanding, and 15 of 55 on coping; 0 minutes on decision making and planning or referrals). There were limitations to this analysis; most of the patients were white, there were risks of a lack of generalizability outside of a major academic cancer center, potential recall bias, and some overlap in domains of care; also, the analysis measured the length of time of the first visit only.

A qualitative substudy of the 2010 Temel et al² report by Yoong et al²⁴ included 77 participants and aimed to identify the content and key elements of early palliative care for outpatients and look for variation in elements over time. The methods included analyzing and coding documentation to look for themes. The following major themes were identified: relationship and rapport building, addressing symptoms, addressing coping, establishing illness understanding, discussing cancer treatments, EOL planning, and engaging family members; initial visits emphasized the first, fourth, and fifth themes, and later visits emphasized the fifth and sixth themes. Visits throughout the trajectory included the second, third, fourth, and seventh themes. Another substudy of the Temel et al report by Back et al²¹ was a qualitative study suggesting that these timings are a result of deliberate strategies of palliative care clinicians. In the small randomized trial of the Breathlessness Intervention Service for patients with lung cancer described under Clinical Question 1, additional support, personal touch, and the way information was presented over time were highly valued because they increased patient and caregiver confidence.¹⁵

Chochinov et al¹² conducted the first RCT of dignity therapy. This three-arm RCT randomly assigned 326 participants with prognoses of 6 months or less to dignity therapy (defined as a form of psychotherapy "enhancing the end-of-life experiences of terminally ill patients"^{12(p753)}), standard palliative care, or client-centered care (defined as a supportive psychotherapeutic approach, in which

a “research nurse therapist guides the patient through discussions that focus on here-and now issues—ie, participants are asked about their illness, associated symptoms, and what is being done to address their distress”^{12(p755)}). Dignity therapy is intended to generate “a sense of meaning, purpose, continued sense of self, and overall sense of dignity.”^{12(p754)} The primary outcomes were in the domain of distress (psychosocial, emotional, and spiritual), which were measured before and after the interventions. No statistically significant differences were found among the three arms. In a poststudy survey, there were statistically significant improvements in QOL with dignity therapy versus the two other arms, as there were in mental health. There were no such differences in symptoms or survival. There was statistically significant improvement in dignity with regard to family relationships. In the comparison of the three arms, senses of sadness and depression and satisfaction outcomes were statistically significantly higher with dignity care than with palliative care. Spiritual well-being was also statistically significantly improved compared with client-centered care.

Clinical interpretation. Palliative care in oncology is conceptualized as a critical component of care that addresses the QOL needs of the patient and his or her family and helps the patient to establish his or her goals and preferences for care (Clinical Question 5 describes relevant literature on families). Palliative care is complementary to traditional oncology care that focuses on disease-directed therapy to reduce symptom burden from disease and prolong life. The integration of palliative care into standard oncology care soon after diagnosis is of benefit to patients and families (Special Commentary provides further discussion on timing). Early involvement of palliative care does not hinder the provision of oncology services or ask that patients and families discuss and make decisions about EOL care before they are ready (emotionally or from a treatment standpoint) to discuss these topics. Rather, palliative care can complement oncologic plans, helping to ensure patients’ goals are met. To accomplish these aims, palliative care services are individually tailored and have distinct elements that complement the services provided in standard oncology care. These features include an emphasis on the psychosocial challenges of worsening disease and additional time spent in assisting with decision making. Initial palliative care appointments are time intensive, often focused on building rapport with patients and families, establishing illness understanding, and discussing symptoms. Later visits may focus on discussing changes to cancer treatments and EOL issues. Throughout the illness trajectory, palliative care visits address symptom management, patient and family coping, and assessment of illness understanding and seek to engage the patient’s family.

CLINICAL QUESTION 4

How can palliative care services relate in practice to other existing or emerging supportive care services (including nurse navigation, lay navigation, community and home health care, geriatric oncology, psycho-oncology, and pain services)?

Recommendation 4

Among patients with cancer with high symptom burden and/or unmet physical or psychosocial needs, outpatient programs of cancer care should provide and use dedicated resources (palliative care clinicians) to deliver palliative care services to complement existing program

tools (type: informal consensus, benefits outweigh harms; evidence quality: intermediate; strength of recommendation: moderate).

Literature review update and analysis. Back et al²¹ conducted a qualitative substudy of the Temel et al² study with physicians and advanced practice nurses involved in the palliative care of the participants to characterize their approaches (mentioned under Clinical Question 3). The participants identified three primary areas: managing symptoms, emotional work, and serving as an interpreter between the patient and oncologist. This study extends the findings of the Yoong et al²⁴ study, also discussed under Clinical Question 2. One strength of the Back et al study was that the data analysts were not involved in the clinical trial or qualitative study. Limitations included some similar to those in the RCT (eg, single-institution study). In addition, the sample size was small.

Uitdehaag et al¹⁸ performed an RCT of 66 patients with incurable upper GI cancer in the Netherlands and their relatives. The authors compared monthly nurse-led follow-up at home with follow-up at a clinic. Patients were eligible if a panel had determined that cure was not possible and if they were not eligible for (further) antitumor treatment. The primary outcome was HRQOL, and additional outcomes included satisfaction and cost. The study found some statistically significant differences in the satisfaction items, including advice and information given by the care provider and patient involvement in care planning. The HRQOL results were similar between the two groups. Satisfaction and lower burden were reported by patients and their relatives in the intervention arm. Costs per patient with the nurse-led intervention were 38% lower than with clinic visits; however, there were more visits in this group. Although the services were available for up to 13 months, most data were analyzed at 4 months because of participant dropout (at 4 months: intervention, 70% dropout; control, 75%). The authors discussed several limitations, including participant dropout and a potential lack of generalizability. The Chochinov et al¹² study discussed under Clinical Question 3 is also relevant to this section. However, there is a paucity of comparative health research studies to inform how palliative should work with other existing or emerging supportive care services, and the panel suggests research be conducted on these topics.

Clinical interpretation. As of the most recent guideline, new literature has emerged to better understand the importance of service delivery provided by palliative care clinicians. Among most studies, the most frequent clinicians providing service delivery or palliative care intervention were nurses. However, despite two randomized trials outlining palliative care interventions specifically delivered by nurses,^{12,18} some results show limited benefits, either because of noncompletion by patients or early dropout. Trials did identify improved QOL benefits as a direct result of palliative care interventions, but none of the trials compared whether palliative care programmatic interventions differed from other service program tools or whether they were superior. The data are clear that added palliative care services complement usual oncology care and enhance benefits to patients across the continuum.

Outpatient programs of cancer care often deliver services to address high symptom burden or unmet current or anticipated physical or psychosocial needs through program tools such as nurse navigation, geriatric oncology, or pain services during early phases of care and transition patients to palliative care programs in late phases of care

(EOL care planning). Other professionals serving these patients and their caregivers include social workers, mental health professionals, clergy members, integrative oncology providers, and more. Offering palliative care across the continuum should complement existing supportive care programs (eg, social work, pain management, pastoral care) and may serve to ensure coordination and communication across these services.

CLINICAL QUESTION 5

Which interventions are helpful for family caregivers?

Recommendation 5

For patients with early or advanced cancer for whom family caregivers will provide care in outpatient, home, or community settings, nurses, social workers, or other providers may initiate caregiver-tailored palliative care support, which could include telephone coaching, education, referrals, and face-to-face meetings. For family caregivers who may live in rural areas and/or are unable to travel to clinic and/or longer distances, telephone support may be offered (type: evidence based; evidence quality: low; strength of recommendation: weak).

Literature review update and analysis. The Dionne-Odom et al¹³ study was part of the ENABLE III RCT of early versus delayed initiation of palliative care in a rural area. Dionne-Odom et al included 122 caregivers of patients with advanced cancer. The family caregiver intervention consisted of telephone coaching sessions and included education and coaching by nurses. The primary outcomes studied were QOL, depressed mood, and burden of caregivers. There was a significant benefit in the depression end point with early palliative care. The investigators conducted an intention-to-treat analysis with a terminal-decline model (data from last 36 weeks of life). This analysis also found a benefit in depression and stress but not in QOL or objective or demand burden scores. Limitations included a lower sample size than planned, in addition to an attrition rate greater than 30%. Therefore, the results may not be generalizable to other populations.

Hudson et al¹⁷ reported the results of a 4-week, three-arm RCT of family caregivers caring for their loved ones with advanced cancer at home. It compared face-to-face visits (one or two) by nurses with standard care and included 148 participants. The intervention involved assessment, a guidebook, telephone or home visit(s), a care plan, and bereavement preparation. The primary outcome was psychological well-being at three time points, and secondary outcomes included preparedness for and positive aspects of caregiving and caregiver competence at the same time points. Most of the effects were small and nonsignificant, including for the primary outcome (General Health Questionnaire). There was a small and significant change in the preparedness scale with two visits, and caregiver competence was significantly better for both one and two visits. Limitations included a small sample size and short intervention time.

The Sun et al⁴ study was a nonrandomized, sequential quasi-experimental study of patients with stage I to IV NSCLC along with the patients' family caregivers (accompanying the corresponding study reporting on patient outcomes by Ferrell et al²⁰). Data from 366 family caregivers were analyzed. The intervention included professionals from multiple professions who, after multidisciplinary team meetings, provided referrals, educational sessions, and self-care plans to family caregivers. The outcomes were primarily QOL outcomes, as well as

psychological distress, caregiver burden, and caregiving skills preparedness; the participants were observed for 6 months. The 12-week measurement was the primary outcome. Those who received the intervention had significantly lower caregiver burden (for some subscales; $P < .001$) and stress ($P = .008$) than the comparator group. Total QOL and two of the subdomains were not statistically significantly different. There were statistically significant differences in the social and spiritual well-being and psychological distress measurements. There were no statistically significant differences in caregiver skills preparedness.

Summary of outcomes. Only one published study found statistically significant differences for family caregivers in the QOL outcomes for the palliative care group. Published studies found statistically significant differences in some mental health outcomes, including depression (one study), stress (three studies), caregiver burden (three studies), and psychological distress. There were varying findings in preparedness outcomes.

Clinical interpretation. Early palliative care involvement may benefit family caregivers emotionally and psychologically by lowering levels of depression, stress, caregiver burden, and psychological distress. Nurses and other members of the health care team may offer support and education through structured, face-to-face, and telephone sessions. Contents of these sessions could include education and the development of self-care plans. The decision to offer face-to-face versus telephone encounters can take into account the family caregivers' unique situations (eg, distance from clinic). FGCs may also benefit from referrals to supportive care services and community resources. Outcomes in studies were attained in three to four sessions, making these feasible interventions to implement. There is insufficient evidence on the long-term effects of these interventions. There is stronger evidence supporting the benefit of these interventions for family caregivers of patients with advanced cancer^{4,13,17} than for those of patients with early-stage cancer.⁴

CLINICAL QUESTION 6

Which patients should be offered or referred to palliative care services, and when in their disease trajectory; are there triggers that should be used to prompt specialty palliative care referrals?

Special Commentary

The patient populations in the palliative care intervention studies that have demonstrated improvements in patient and family outcomes may help identify appropriate triggers to specialty palliative care referrals. Most studies have been conducted among outpatients with advanced-stage malignancies and their families, although the study by Ferrell et al²⁰ included patients with all stages of NSCLC, with QOL improvements found to be greater among patients with early- as compared with late-stage disease. Furthermore, the timing of palliative care interventions provides guidance regarding optimal timing of referrals. The benefits of palliative care referrals at the time of diagnosis of advanced malignancies are supported by studies demonstrating improved outcomes with early palliative care interventions versus usual care. These include the RCT of early palliative care (ie, at the time of diagnosis) versus usual care by Temel et al² in patients with advanced-stage lung cancer in the outpatient setting and the cluster randomized trial by Zimmermann et al¹⁹ of early palliative care versus standard care for patients advanced solid

tumors as outpatients with a physician-assessed limited prognosis (ie, 6 to 24 months). Additionally, some studies comparing early versus delayed palliative care referrals in the setting of advanced-stage malignancies suggest that benefits may be greater when referrals occur earlier.^{13,14} Notably, the study by Bakitas et al¹¹ of early (30 to 60 days within diagnosis) versus delayed specialty palliative care referrals (3 months after the early group) did not find differences between arms in patient QOL outcomes or resource use, but it observed significantly improved 1-year survival in the early palliative care group. A retrospective cohort study published after the closing data parameter of the systematic review conducted for this guideline compared matched patients with cancer who received early (80% outpatient) versus late (80% inpatient) palliative care consultation and found early palliative care was associated with less intensive medical care, improved quality outcomes, and approximately \$6,000 in cost savings per person at EOL for patients.³¹

Investigations of specific triggers for palliative care referrals are limited, especially regarding outpatient palliative care (where the studies showing benefit were conducted).^{2,11,19,20} One study, which did not meet the ASCO systematic review criteria, piloted a checklist and used it to prompt palliative care referrals among patients who were hospitalized, including those with cancer.³² In this study, palliative care referrals were triggered for hospitalized inpatients meeting one or more of the following criteria: stage IV disease or stage III lung or pancreatic cancer, prior hospitalization in the last 30 days, hospitalization longer than 7 days, and uncontrolled symptoms. The pilot population, compared with an inpatient population meeting those criteria in the year before the intervention, had improvements in 30-day readmission rates and mortality index³² (mortality index is observed ν expected deaths³³).

However, these criteria for palliative care referral alone would likely overwhelm current palliative care resources and point to the need for improved generalist palliative care competencies among oncologists to ensure basic palliative care needs are addressed. Additionally, as suggested by the findings of Ferrell et al,²⁰ these criteria would not identify patients with earlier-stage cancer in need of palliative care referrals. This implies the need for triggers for specialty palliative care referrals to be assessed early and regularly among all patients with cancer, regardless of disease stage, although most prominently among patients with advanced-stage cancer and their families, and for oncologists to learn primary palliative care skills.³⁴

The Center to Advance Palliative Care,³⁵ in recognition of the critical need for identifying patients in need of subspecialty palliative care referrals, convened a consensus panel in 2010 to aid in defining key triggers for palliative care referrals for patients who are hospitalized. In its statement, the consensus panel first noted that it is “neither sustainable nor desirable that palliative care specialists manage all the palliative care needs of all seriously ill patients.”^{35(p1)} The panel statement pointed to the “urgent need to improve basic palliative care assessment and treatment skills among clinicians caring for patients with serious illness, with the goal of reserving specialty-level palliative care services for problems beyond their capabilities.”^{35(p1)} In addition to promoting primary palliative care through provider education, the consensus panel promoted the application of checklists for palliative care referrals to be used by those caring for patients with serious illness. Criteria that the consensus panel identified, based on review of the literature and Expert Panel

consensus, are intended to apply to the inpatient setting across seriously ill populations, but they are informative to the populations of patients with cancer in both outpatient and inpatient settings (Table 3).

In summary, interventional studies support early specialty palliative care referrals among patients with advanced-stage malignancies and their caregivers. However, additional triggers should be considered among all patients with cancer to ensure prompt referrals to specialty palliative care services for patients at high risk for specialty palliative care needs. Furthermore, oncologists should be educated in primary palliative care competencies and regularly assess triggers for palliative care specialty services as part of their care of patients with cancer and their family caregivers. Additional studies are needed to better define triggers for meeting unmet specialty palliative care needs in the population of patients with cancer.

PATIENT AND CLINICIAN COMMUNICATION

Patient, caregiver, and clinician communication is a foundation of palliative care. Research on patient and clinician communication specific to patients with advanced cancer, including on EOL issues, and other aspects related to palliative care has been performed; however, the scope of this guideline did not include reviewing that literature. However, a key component in retrospective analyses has been the performance of a goals-of-care discussion that entails asking about knowledge of the illness, realistic options for treatment, and planning for the future; if such discussions are held, care at EOL improves and is more consonant with patient preferences.

ASCO is developing a future guideline on patient–physician communication. In addition, several previous versions of the ASCO guideline on the treatment of patients with stage IV NSCLC reviewed literature relevant to that population and provided concrete communication tips for clinicians, including to discuss the risks and benefits of antitumor treatment and palliative care with patients and to talk over prognosis, clinical trials, and advanced care planning.⁵ The stage IV NSCLC guideline also suggests inquiry about psychological and spiritual care, social support, assessing family caregiver needs, and physician self-care. Please see the Palliative Care and Patient and Clinician Communications sections of the 2015 guideline, as well as its Data Supplement, which includes sample talking points.⁵

HEALTH DISPARITIES

Although ASCO clinical practice guidelines represent expert recommendations on the best practices in care to provide the highest level of cancer care, it is important to emphasize that many patients have limited access to palliative care. Racial and ethnic disparities in health care contribute significantly to this problem in the United States. Patients with cancer who are members of racial or ethnic minorities disproportionately experience comorbidities, encounter more substantial obstacles to receiving care, are more likely to be uninsured, and are at greater risk of receiving care of poorer quality than other Americans.³⁶⁻³⁹ Many other patients lack access to care because of their geographic location or distance from appropriate treatment facilities.

Table 3. Criteria for Palliative Care Assessment at Time of Admission³⁵

| Criterion* |
|---|
| <p>Primary†</p> <p>Surprise question: You would not be surprised if patient died within 12 months or before adulthood²³⁻²⁵</p> <p>Frequent admissions (eg, > one admission for same condition within several months)²⁶⁻³⁰</p> <p>Admission prompted by difficult-to-control physical or psychological symptoms (eg, moderate to severe symptom intensity for > 24 to 48 hours)^{6,31}</p> <p>Complex care requirements (eg, functional dependency; complex home support for ventilator, antibiotics, feedings)⁶</p> <p>Decline in function, feeding intolerance, or unintended decline in weight (eg, failure to thrive)^{6,31}</p> |
| <p>Secondary‡</p> <p>Admission from long-term care facility or medical foster home§</p> <p>Elderly patient, cognitively impaired, with acute hip fracture^{32,34-36}</p> <p>Metastatic or locally advanced incurable cancer³⁷</p> <p>Chronic home oxygen use§</p> <p>Out-of-hospital cardiac arrest^{38,39}</p> <p>Current or past hospice program enrollee§</p> <p>Limited social support (eg, family stress, chronic mental illness)§</p> <p>No history of completing advance care planning discussion or document^{6,31}</p> |
| <p>NOTE. Adapted with permission.³⁵</p> <p>*In addition to potentially life-limiting or life-threatening condition.</p> <p>†Primary criteria are global indicators that represent minimum that hospitals should use to screen patients at risk for unmet palliative care needs.</p> <p>‡Secondary criteria are more-specific indicators of high likelihood of unmet palliative care needs and should be incorporated into systems-based approach to patient identification if possible.</p> <p>§These indicators are included based on panel consensus opinion.</p> |

As discussed in a review by Johnson et al⁴⁰ from 2013, there is a paucity of health disparities research on palliative care, and several limitations exist to the research that has been conducted. Of a limited number of publications, some indicate similar benefits for people of color and whites, and others show that disparities exist, as in other aspects of cancer care (described in the ASCO stage IV NSCLC guideline⁵). In addition to race, poverty and low socioeconomic and/or immigration status are determinants of barriers to palliative care; in both areas, clinician–patient communication gaps occur.^{41,42} One example of a disparity was found in a 2010 prospective longitudinal cohort study of black and white patients with advanced cancer conducted by Mack et al,⁴³ who examined the differences in how patients and physicians communicate about EOL care by race. The investigation was based on the observation that some black patients receive more life-prolonging EOL care than some white patients. The study confirmed this observation; despite the same rates of communication, there was an association between lower rates of life-prolonging care among white patients and discussions about life-prolonging care, suggesting there are contributing factors occurring in both communication and the health system. An exception was improvement in discussions leading to increased use of hospice among some black patients.

Another study showed dissemination of information about palliative and EOL care may not reach some black audiences in the United States at all. Fishman et al⁴⁴ performed a content analysis of cancer news intended for black audiences or nonspecific audiences to find discussions of palliative care–related topics, including adverse events, EOL care, or palliative or hospice care. The authors found statistically significantly lower reporting on adverse events, treatment failure, and death and dying in black American media. The authors found zero articles on palliative care or hospice in the media directed at black audiences.

Studies have shown that patients covered by Medicaid in the United States have not received guideline- or quality-adherent palliative care (eg, receipt of chemotherapy at EOL; v those with Medicare).^{45,46} Geographic disparities in the receipt of palliative

care also occur, including in rural versus urban or metropolitan areas, as shown in studies from multiple countries.⁴⁷⁻⁴⁹ One pilot study found a possible beneficial intervention (ie, using videoconferencing to provide palliative care).⁴⁸ Recent work has shown that African Americans are at least as likely as whites to be referred for inpatient palliative care consultation, live longer than whites after consultation (25 v 17 days), and have a rate of hospice use that exceeds that of whites (59% v 51%).⁵⁰ Palliative care consultation seems to allow providers to bring up advance directives and do-not-resuscitate status (eg, with 98% of African Americans at one hospital; 65% agreed to do-not-resuscitate orders).^{51,52} In addition, palliative care consultation with specific emphasis on goals of care discussion seems to level the playing field, with the same number of African Americans electing hospice as white patients; in one study, those who discussed code status had twice the rate of referral to hospice (odds ratio, 2.14).⁵³

In the studies underlying the recommendations in this update, white participants were primarily overrepresented (ie, 71% to 97%). Clearly, further research involving people of color and/or with lower socioeconomic status and/or participants from other under-represented groups is needed. It is not within the scope of this guideline to examine specific factors contributing to disparities; however, given the relatively recent publication of research and guidelines on palliative care, it is likely that dissemination is occurring slowly, especially in populations already experiencing health disparities and/or populations with cultures differing from those included in research to date. Awareness of the disparities in access to palliative care should be considered in the context of this clinical practice guideline, and health care providers should strive to deliver the highest level of cancer care to these vulnerable populations.

MULTIPLE CHRONIC CONDITIONS

Creating evidence-based recommendations to inform treatment of patients with additional chronic conditions, a situation in which

a patient may have two or more such conditions—referred to as multiple chronic conditions (MCCs)—is challenging. Patients with MCCs comprise a complex and heterogeneous population, making it difficult to account for all of the possible permutations to develop specific recommendations for care. It is important to note that elderly patients most often have multiple chronic illnesses, and with the aging population, it is expected that this problem will increase. In addition, the best available evidence for treating index conditions, such as cancer, is often from clinical trials, the study selection criteria of which may exclude these patients to avoid potential interaction effects or confounding of results associated with MCCs. As a result, the reliability of outcome data from these studies may be limited, thereby creating constraints for expert groups to make recommendations for care in this heterogeneous patient population. One recently published report noted that palliative care consultation in the hospital was associated with a marked reduction in direct costs (14% to 22%, depending on when the consultation occurred) and that the effect was more pronounced when the patient had more comorbidities; clinical outcomes were not reported.⁵⁴

Because many patients for whom guideline recommendations apply present with MCCs, all treatment plans need to take into account the complexity and uncertainty created by the presence of MCCs and highlight the importance of shared decision making regarding guideline use and implementation. Therefore, in consideration of recommended care for the target index condition, clinicians should review all other chronic conditions present in patients and take those conditions into account when formulating treatment and follow-up plans.

In light of these considerations, practice guidelines should provide information on how to apply the recommendations for patients with MCCs, perhaps as a qualifying statement for recommended care. This may mean that some or all of the recommended care options are modified or not applied, as determined by best practice in consideration of any MCC.

COST IMPLICATIONS

How Is Palliative Care Reimbursed?

Palliative care is reimbursed as a medical specialty comparable to oncology or hematology. Hospice and palliative medicine was made an official medical subspecialty in the United States in 2006 and received a Medicare billing identifier in 2008. Physicians and advance nurse practitioners can bill for Medicare professional time and palliative care services, but other members of interdisciplinary teams, such as chaplains and social workers, cannot bill for palliative care services directly, so some other provision must be made for them.

What Other Resources Are Available to Support Palliative Care? What Is the Business Case for Palliative Care?

The primary impetus for hospice and subsequently palliative care was to improve QOL and symptom management. Hospice has been proven over many years to improve symptoms, reduce patient and caregiver distress, produce equal or even better survival compared with those who do not use hospice, and improve the chance of

dying where one desires, usually at home. Putting in place a system of care that can respond to symptoms produces the positive effect of reductions in the number of hospitalizations near EOL. The net result is a savings of more than \$8,600 per Medicare beneficiary.⁵⁵

The primary argument for palliative care has always been to improve care for patients and families. However, a compelling case can be made that palliative care is better care at a cost we can afford; palliative care in most studies has actually reduced the total cost of care, often substantially.⁵⁶ Not a single study, randomized or observational, has shown that cost is increased.⁵⁷ The first large randomized trials of usual care versus usual care plus an interdisciplinary palliative care team were conducted by a vertically integrated health care organization—Kaiser-Permanente—involving more than 800 patients. Avoided hospital and intensive care unit days in the last month of life led to equal survival, better satisfaction and communication, and cost savings of $-\$7,550$ ⁵⁸ and $-\$4,885$ ⁵⁹; the savings were sufficient to convince Kaiser-Permanente to have interdisciplinary palliative care teams at all its major sites. Similar savings were observed at eight centers, with 14% direct cost savings in discharges of living patients ($-\$2,374$ in 2014 dollars) and 22% direct cost savings for decedent discharges ($-\$6,871$ in 2014 dollars).^{60,61} The Veterans Administration also observed 38% direct cost savings for patients receiving palliative care, overall, compared with matched patients who did not receive palliative care, which led it to emphasize palliative care across its systems.⁶¹

It is important to consider the type of palliative care intervention. Inpatient palliative care consultation, often conducted when a patient has a short time to live and many symptoms, improves care and reduces costs. If palliative care consultation occurs while the patient is an inpatient, the 30-day readmission rate is cut from 15% to 10%. If, during that consultation, a goals-of-care discussion is conducted, the 30-day readmission rate risk is 36% of that if the discussion is not held.⁶²

One way that costs are reduced is through increased and earlier referrals to hospice. If the palliative care team saw patients who were hospice eligible at Johns Hopkins Hospital, 57% of them went home with hospice; if the palliative care team did not see them, only 27% went home with hospice.⁶³ Similar results were seen in a hospital-hospice partnership, with a five-fold reduction in 30-day readmissions (1% v 5%).⁶⁴ Patients who received a palliative care team consultation were 3.24 times more likely to be discharged to hospice ($P < .001$), 1.52 times more likely to be discharged to a nursing facility, and 1.59 times more likely to be discharged home with services ($P < .001$).⁶⁵ Among patients in New York with Medicaid, referrals to hospice increased more than 10-fold if the palliative care team saw the patient.⁶⁶

Going home with hospice meant a 5% 30-day readmission rate versus a 25% rate for matched patients who did not go home with hospice.⁶⁷ Palliative care for those with life-limiting illnesses should help make the transition to hospice easier and sooner before death. It is important to point out that patients who use hospice, compared with those who do not use hospice, have markedly improved symptoms, less caregiver distress, reduced costs of approximately \$8,700 per Medicare beneficiary,⁵⁵ and, according to two published reports, actually live longer.^{68,69}

Inpatient palliative care also reduces costs directly by reducing the length of stay in hospital and the services that are provided, again with no impact on survival. Inpatient palliative care during

hospitalization reduces direct hospital costs by 14% to 24%. The earlier the palliative care consultation occurs, the larger the cost savings.^{54,70} The economic impact of concurrent outpatient care has been less marked, but it is notable that no study has shown increased costs for patients with cancer.

In the 2010 Temel et al² lung cancer study, costs for the two arms were essentially equal; the early palliative care group had a lower mean cost per day of \$117, but patients in this arm lived 98 days longer.⁷¹ The palliative care breathlessness study involving patients with advanced cancer showed both less dyspnea and lower costs with palliative care, with a 66% to 81% chance of palliative care being cost saving.²⁷ The recent announcement of the Medicare Choices program that allows concurrent hospice care and usual cancer care for patients who are hospice eligible is an endorsement of these potential cost savings. This program is based on the Aetna Compassionate Care program that showed increased hospice referrals and a 22% savings in the last 40 days of life for patients with cancer, with no obvious effect on survival.⁷² In contrast, the outpatient concurrent care models here have shown a more limited impact on the cost of care. Farquhar et al²⁷ showed that early palliative care for patients with cancer was not only effective but reduced costs. All the studies reported here have shown improved care, but not a single one has reported increased costs.

EXTERNAL REVIEW AND PUBLIC COMMENT

The draft recommendations were released to the public for open comment from July 6 to 20, 2016. A total of 94% of the 28 respondents either agreed or agreed with slight modifications to the recommendations, whereas 6% of the respondents disagreed. Comments received were reviewed by the Expert Panel and integrated into the final draft before approval by the ASCO Clinical Practice Guideline Committee.

GUIDELINE IMPLEMENTATION

ASCO guidelines are developed for implementation across health settings. Barriers to implementation include the need to increase awareness of the guideline recommendations among front-line practitioners and patients with cancer and their caregivers, as well as the need to provide adequate services in the face of limited resources. A retrospective quality-of-care survey of caregivers by Teno et al⁷³ found that between 2000 and 2011 to 2013, caregivers' reports of their deceased loved ones' needs for many aspects of palliative and EOL care showed perceptions worsening or staying the same over time, regardless of large policy changes. The only improvement was seen in religious and spirituality needs among all respondents, and in a subanalysis of one of three survey rounds, 61% of those in hospice in their last month of life rated care as excellent versus 47% of those not in hospice. The authors conclude that opportunities for better pain management, better care for dyspnea and anxiety or depression, and better communication remain. Continued focus on implementation and quality measurement in palliative care is crucial.⁷³ This guideline will be distributed widely through the ASCO Practice Guideline Implementation Network (PGIN). The guideline Bottom Line Box is designed to facilitate implementation of recommendations. ASCO guidelines are posted on the ASCO Web site

and most often published in *Journal of Clinical Oncology* and *Journal of Oncology Practice*.

LIMITATIONS OF THE RESEARCH

Research to date has made great strides, but some of the studies faced limitations, such as:

- The field of palliative care research began relatively recently.
- Research funding for palliative care has been limited; therefore, outcome data are limited (90% of hospitals have funding for palliative care services, but few have funding for research).
- The majority of the research has been in patients with solid tumors, and more research is needed across tumor types and in hematology.
- Research in health disparities in palliative care is lacking.
- Some studies were conducted at single sites, which can limit generalizability, and/or had small sample sizes and/or short follow-up.

ASCO believes that cancer clinical trials are vital to informing medical decisions and improving cancer care and that all patients should have the opportunity to participate. Patients in clinical trials may benefit from the support of palliative care.

LIMITATIONS OF THE LITERATURE AND FUTURE DIRECTIONS

To enhance and strengthen the evidence base on palliative care, the dissemination of research results, and the quality and equity of palliative care, more research is needed; specific areas include:

- Identification of the specific elements, such as skills and personnel, resulting in the difference seen in research.
- Identification of triggers for palliative care.
- Inclusion of patients with cancers of types not represented in earlier trials, especially hematologic cancers.
- More research on the role of palliative care for patients with early-stage disease.
- Elucidation of health disparities specific to palliative care to identify disparities, barriers, determinants in receipt and quality of palliative care, and evidence-based interventions to address disparities.
- More research on family caregivers.
- Inclusion of patients with advanced cancer in early-phase clinical trials.

ADDITIONAL RESOURCES

More information, including a Data Supplement with additional evidence tables, a Methodology Supplement with information about evidence quality and strength of recommendations, slide sets, and clinical tools and resources, is available at www.asco.org/palliative-care-guideline and www.asco.org/guidelineswiki. Patient information is available at www.cancer.net. Visit www.asco.org/guidelineswiki to provide comments on the guideline or to submit new evidence.

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Disclosures provided by the authors are available with this article at www.jco.org.

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Integration of Palliative Care Into Standard Oncology Care: American Society of Clinical Oncology Clinical Practice Guideline Update

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Appendix

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| Erin R. Alesi, MD | Virginia Commonwealth University Health System, Richmond, VA | Medical oncology, hematology, and palliative care |
| Tracy A. Balboni, MD | Dana-Farber Cancer Institute, Boston, MA | Radiation oncology |
| Ethan M. Basch, MD | University of North Carolina, Chapel Hill, NC | Medical oncology |
| Janice I. Finn, PhD, LMSW | University of Michigan Health System, Ann Arbor, MA | Palliative care social work |
| Judith A. Paice, PhD, RN | Northwestern University, Evanston, IL | Oncology nursing and pain |
| Jeffrey M. Peppercorn, MD, MPH | Massachusetts General Hospital, Boston, MA | Medical oncology and hematology |
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| Florian Strasser, MD | Cantonal Hospital, St Gallen, Switzerland | Medical oncology and palliative care |
| Jennifer S. Temel, MD | Massachusetts General Hospital, Boston, MA | Thoracic oncology |
| Camilla Zimmermann, MD | Princess Margaret Cancer Centre, Toronto, Ontario, Canada | Palliative care and research |

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| Organization | Web Site |
|--|---|
| Palliative Care Research Cooperative Group | http://www.palliativecareresearch.org |
| National Consensus Project | http://www.nationalconsensusproject.org/ |
| National Palliative Care Research Center | http://www.npcrc.org/content/25/Measurement-and-Evaluation-Tools.aspx |
| Center to Advance Palliative Care | https://www.capc.org/ |
| Patient Reported Outcomes Measurement Information System | https://commonfund.nih.gov/promis/index |