

Evidence-Based Interventions to Improve the Palliative Care of Pain, Dyspnea, and Depression at the End of Life: A Clinical Practice Guideline from the American College of Physicians

Amir Qaseem, MD, PhD, MHA; Vincenza Snow, MD; Paul Shekelle, MD, PhD; Donald E. Casey Jr., MD, MPH, MBA; J. Thomas Cross Jr., MD, MPH; and Douglas K. Owens, MD, MS, for the Clinical Efficacy Assessment Subcommittee of the American College of Physicians*

Recommendation 1: In patients with serious illness at the end of life, clinicians should regularly assess patients for pain, dyspnea, and depression. (Grade: strong recommendation, moderate quality of evidence.)

Recommendation 2: In patients with serious illness at the end of life, clinicians should use therapies of proven effectiveness to manage pain. For patients with cancer, this includes nonsteroidal anti-inflammatory drugs, opioids, and bisphosphonates. (Grade: strong recommendation, moderate quality of evidence.)

Recommendation 3: In patients with serious illness at the end of life, clinicians should use therapies of proven effectiveness to manage dyspnea, which include opioids in patients with unrelieved dyspnea and oxygen for short-term relief of hypoxemia. (Grade: strong recommendation, moderate quality of evidence.)

Recommendation 4: In patients with serious illness at the end of life, clinicians should use therapies of proven effectiveness to manage depression. For patients with cancer, this includes tricyclic antidepressants, selective serotonin reuptake inhibitors, or psychosocial intervention. (Grade: strong recommendation, moderate quality of evidence.)

Recommendation 5: Clinicians should ensure that advance care planning, including completion of advance directives, occurs for all patients with serious illness. (Grade: strong recommendation, low quality of evidence.)

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For author affiliations, see end of text.

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Palliative care at the end of life involves meeting the physical, psychological, social, and practical needs of patients and caregivers. *End of life* is defined as a phase of life when a person is living with an illness that will worsen and eventually cause death. It is not limited to the short period of time when the person is moribund (1). Good clinical care can prevent or alleviate suffering for many patients at the end of life by assessing symptoms and providing psychological and social support to the patients and their families.

The purpose of this guideline is to present the available evidence to improve palliative care at the end of life. This guideline does not address any other settings of palliative care at the end of life. The target audience for this guideline is all clinicians caring for patients needing end-of-life care. The target patient population is everyone with seriously disabling or symptomatic chronic conditions at the end of life. These recommendations are based on the systematic evidence review in the background paper in this issue by Lorenz and colleagues (1), which is based on an Agency for Healthcare Research and Quality (AHRQ) evidence report (2).

End-of-life care has been identified by the Institute of

Medicine as one of the priority areas to improve quality of health care (3). The Institute of Medicine report identified specific gaps related to end-of-life care, such as pain control in advanced cancer and care for patients with advanced organ failure. High-quality evidence on end-of-life care is limited, and most of the evidence is derived from the literature that focused on patients with cancer; therefore, this guideline does not address many important aspects of end-of-life care. For example, nutritional support, complementary and alternative therapies, and spiritual care were not part of the review. If an end-of-life intervention is not addressed in this guideline, it does not mean that no ben-

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*This paper, written by Amir Qaseem, MD, PhD, MHA; Vincenza Snow, MD; Paul Shekelle, MD, PhD; Donald E. Casey Jr., MD, MPH, MBA; J. Thomas Cross Jr., MD, MPH; and Douglas K. Owens, MD, MS, was developed for the Clinical Efficacy Assessment Subcommittee of the American College of Physicians (ACP); Douglas K. Owens, MD, MS (*Chair*); Donald E. Casey Jr., MD, MPH, MBA; J. Thomas Cross Jr., MD, MPH; Paul Dallas, MD; Nancy C. Dolan, MD; Mary Ann Forcica, MD; Lakshmi Halasyamani, MD; Robert H. Hopkins Jr., MD; and Paul Shekelle, MD, PhD. Approved by the ACP Board of Regents on 14 July 2007.

Table. The American College of Physicians' Guideline Grading System*

Quality of Evidence	Strength of Recommendation	
	Benefits Clearly Outweigh Risks and Burden OR Risks and Burden Clearly Outweigh Benefits	Benefits Finely Balanced with Risks and Burden
High	Strong	Weak
Moderate	Strong	Weak
Low	Strong	Weak
Insufficient evidence to determine net benefits or risks	I-recommendation	

* Adopted from the classification developed by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) workgroup.

efit is related to that particular intervention, but it indicates that the intervention has not been sufficiently studied to demonstrate efficacy. Some important topics in end-of-life care, such as interpersonal and social interventions, may be especially difficult to study. The American College of Physicians' End-of-Life Care Consensus Panel has a series of papers related to ethical issues around end-of-life care that can be accessed from its Web site (www.acponline.org/ethics/papers.htm).

METHODS

The literature search for this guideline included studies from MEDLINE and reviews of cancer, congestive heart failure, and dementia from the Database of Abstracts of Reviews of Effects from January 1990 to November 2005. Citations from the nonsystematic literature were taken from the review by the National Consensus Project for Quality Palliative Care (4). The review included only English-language publications from the United States, Canada, Western Europe, Australia, and New Zealand. Details about the methods used for the systematic evidence review may be found in detail in the background paper in this issue (1).

The objective for this guideline was to answer the following questions:

1. What are the critical elements for clinicians to address when caring for persons coming to the end of life?
2. What do definitions of the *end of life* suggest about identifying patients who could benefit from palliative approaches?
3. What treatment strategies work well for pain, dyspnea, and depression?
4. What elements are important in advance care planning for patients coming to the end of life?
5. What elements of collaboration and consultation are effective in promoting improved end-of-life care?
6. What elements of assessment and support are effective for serving caregivers, including family, when patients are coming to the end of life?

This guideline grades the evidence and recommendations using the American College of Physicians' clinical practice guidelines grading system, adopted from the classification developed by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) workgroup (Table).

CRITICAL ELEMENTS FOR END-OF-LIFE CARE

There is a wide range of critical elements for patients nearing the end of life, as well as for their caregivers. Preventing and treating pain and other symptoms; supporting families and caregivers; ensuring the continuity of care; ensuring respect for persons and informed decision making; attending to well-being, including existential and spiritual concerns; and supporting function and survival duration are general issues that are common for most end-of-life care patients (4–11).

IDENTIFYING PATIENTS WHO COULD BENEFIT FROM PALLIATIVE APPROACHES

The literature review did not identify any evidence-based tools that have been validated and shown to predict the optimal timing to initiate palliative care services. Decisions to initiate palliative care at the end of life should be individualized on the basis of patient symptoms and preferences.

TREATMENT STRATEGIES

Pain

Strong evidence from trials of patients with cancer supports the use of nonsteroidal anti-inflammatory drugs, opioids, bisphosphonates, and radiotherapy or radiopharmaceuticals for pain (12). Bisphosphonates are specifically effective for bone pain. However, head-to-head comparisons of specific drugs or reports on delivery strategies are difficult to do because of methodological issues and heterogeneity (12). Evidence was insufficient to assess the usefulness of exercise or acupuncture in pain management (13, 14).

A meta-analysis that included 43 studies showed that palliative care teams are modestly beneficial in providing care for pain management compared with usual care teams (effect size, 0.13 SD [95% CI, 0.11 to 0.63 SD]) (15). Other studies that evaluated quality of life showed no difference (16) and no effect of palliative care consultation (in contrast to palliative care teams) on pain scores (17).

Dyspnea

Evidence from 13 studies shows a valuable effect of morphine for dyspnea in advanced lung disease (standardized mean difference, -0.31 [CI, -0.50 to -0.13]) (18). This is also supported by other studies that show the benefits of morphine for treating dyspnea in advanced lung disease and terminal cancer (19, 20). However, using nebulized opioids compared with oral opioids showed no ad-

ditional benefit. Also, 1 study showed that dihydrocodeine resulted in a statistically but not clinically significant increase in PCO_2 during treatment (18). Good-quality evidence shows that long-acting β -agonists are beneficial in the treatment of dyspnea in chronic obstructive pulmonary disease (21).

Twelve studies evaluated various interventions for reducing dyspnea in patients with chronic obstructive pulmonary disease, heart failure, cancer, or all conditions. Evidence was mixed when comparing oxygen therapy with room air. One study showed better oxygen saturation, respiratory effort and rate, and dyspnea with oxygen (19). However, Bruera and colleagues (20) showed no difference in dyspnea and fatigue between oxygen and air after a 6-minute walk test.

Studies that evaluated service delivery showed no effect of facilitated patient-provider communication or palliative care consultation for dyspnea treatment (16, 17, 22, 23).

Depression

Good evidence supports the effectiveness of long-term use of tricyclic antidepressants or selective serotonin reuptake inhibitors, as well as psychosocial interventions (education, cognitive and noncognitive behavioral therapy, informational interventions, and individual and group support) for treating patients with cancer who have depression (12).

Gysels and Higginson (24) identified 15 intervention studies that showed that behavioral interventions were effective in the treatment of depression, whereas 1 complementary medicine intervention was ineffective for depression (24). Evidence for using guided imagery and exercise showed mixed results (13, 25).

Palliative care for outpatients did not have any effect on depression and anxiety, and care coordination showed no effect on depression in patients with cancer near the end of life (22, 23, 26, 27).

IMPORTANT ELEMENTS FOR ADVANCE CARE PLANNING

Research shows that individuals are more likely to use advance directives in the presence of extensive multi-component interventions than with limited interventions (28, 29). One study showed that hospice use increased when goal-oriented interviews and decisions between palliative care facilitators and patients were communicated to nursing home physicians (30). In addition, another study showed an increase in documented treatment limitations and preference-concordant care for patients served by social workers trained in care planning (31). Also, proactive communication from skilled discussants, such as an ethics team, can help reduce utilization of unnecessary services without harming patients or family members (32, 33).

In summary, various processes, such as consulting caregivers, enhancing clear communication, eliciting values, and addressing the emotional context, are important elements for comprehensive advance care planning. Clinicians

should help patients and families plan in advance for likely or important clinical decisions.

COLLABORATION AND CONSULTATION TO IMPROVE END-OF-LIFE CARE

Studies have shown that the following factors improve utilization outcomes and patient-centered outcomes: multidisciplinary teams involving nurses and social services, continuity of care and service coordination, and facilitated communication.

A meta-analysis of 29 randomized, controlled trials done by McAlister and colleagues (34) showed that follow-up by a multidisciplinary team resulted in decreased hospitalizations due to heart failure. In addition, a multidisciplinary approach also improved patients' quality of life and functional status (34, 35). Another intervention study showed that coordination between primary physician and cardiologist, nurse case management, education, and patient and family activation improved quality of life and reduced readmissions and costs (36–39).

Evidence related to interventions to improve continuity of care has shown mixed results. Home-based palliative care coordination has shown limited effectiveness for patients, caregivers, and utilization for supportive cancer care (24). However, a meta-analysis that evaluated intensive in-home care by respiratory nurses with hospital support for chronic obstructive pulmonary disease showed reduced hospital days and costs but no change in hospital readmissions (40).

SUPPORTING CAREGIVERS

Evidence supporting the beneficial effect of palliative care teams for caregivers is mixed, with 2 studies showing small positive effects on caregiver burden, anxiety, and satisfaction (24, 41) and 2 others showing no advantage (42, 43). However, evidence from the REACH (Resources for Enhancing Alzheimer's Caregiver Health) project showed a small but statistically significant treatment effect for caregiver burden (44–49). Results from SUPPORT (Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments) showed improved caregiver satisfaction with communication (50, 51). Also, a hospital-based palliative care consultative service for community oncology patients and providers was associated with improved after-death family satisfaction (52, 53). One study showed that individualized multicomponent interventions may be more beneficial than more limited caregiver interventions (54).

In summary, clinicians should routinely and periodically screen adult caregivers for practical and emotional needs while caring for a patient near the end of life. Periodic screening by caregivers for the patient's supportive needs should be a routine part of care for patients with serious chronic illness.

SUMMARY

Symptom control, continuity in care, and reducing caregiver burdens are critical elements of care for managing patients nearing the end of life. In addition, following appropriate treatment strategies for pain, dyspnea, and depression substantially affect patients' end-of-life experiences. Interventions where advance care planning includes trained facilitators (including palliative care providers), involves key decision makers, and addresses care across settings are beneficial for improving care. Further research on potentially beneficial but understudied interventions, and conditions other than cancer, should be a high priority.

RECOMMENDATIONS

Recommendation 1: In patients with serious illness at the end of life, clinicians should regularly assess patients for pain, dyspnea, and depression. (Grade: strong recommendation, moderate quality of evidence.)

Patients needing end-of-life care may present with substantial symptoms, including pain; discontinuity in care; and substantial caregiver burdens. These concerns are critically important for patients and families coping with serious chronic illnesses. Although each patient and family will require individualized assessment and care, the evidence shows that a set of general issues is shared widely among patients needing end-of-life care. These issues include pain and other symptom management, psychological well-being, care coordination and advance care planning, and caregiver burden. The evidence was classified as moderate quality because it was mostly derived from studies of patients with cancer or cancer-predominant populations in addition to being heterogeneous.

Recommendation 2: In patients with serious illness at the end of life, clinicians should use therapies of proven effectiveness to manage pain. For patients with cancer, this includes nonsteroidal anti-inflammatory drugs, opioids, and bisphosphonates. (Grade: strong recommendation, moderate quality of evidence.)

Clinicians should use specific effective therapies for all patients with acute and chronic pain. Strong evidence supports using nonsteroidal anti-inflammatory drugs, opioids, and bisphosphonates for pain relief in patients with cancer. Bisphosphonates are effective for bone pain relief in patients with breast cancer and myeloma.

Recommendation 3: In patients with serious illness at the end of life, clinicians should use therapies of proven effectiveness to manage dyspnea, which include opioids in patients with unrelieved dyspnea and oxygen for short-term relief of hypoxemia. (Grade: strong recommendation, moderate quality of evidence.)

Opioids should be considered in patients with severe and unrelieved dyspnea, for example, in cancer and cardio-pulmonary disease at the end of life. Clinicians should consider the use of oxygen for hypoxemia for advanced chronic obstructive pulmonary disease. Evidence also sup-

ports the use of β -agonists for treating dyspnea in chronic obstructive pulmonary disease, but this use has not been studied for end-of-life care.

Recommendation 4: In patients with serious illness at the end of life, clinicians should use therapies of proven effectiveness to manage depression. For patients with cancer, this includes tricyclic antidepressants, selective serotonin reuptake inhibitors, or psychosocial intervention. (Grade: strong recommendation, moderate quality of evidence.)

Clinicians should assess for and manage symptoms of depression in patients with serious chronic diseases. For patients with cancer, strong evidence shows that depression should be treated with generally effective therapies, including tricyclic antidepressants, selective serotonin reuptake inhibitors, or psychosocial interventions. Because the strong evidence is derived only from the studies that included patients with cancer and not for all patients at the end of life, it is classified as moderate on average.

Recommendation 5: Clinicians should ensure that advance care planning, including completion of advance directives, occurs for all patients with serious illness. (Grade: strong recommendation, low quality of evidence.)

All care planning must address certain elements, such as surrogate decision makers, resuscitation, and emergency treatment, and should occur as early as possible in the course of serious illness before the end of life. Care planning must anticipate specific issues for each patient's clinical course, for example, the management of dementia, including tube feeding; whether to initiate or continue chemotherapy in patients with cancer; and whether to deactivate implantable cardioverter defibrillators in patients who have intractable congestive heart failure. Care plans should be reassessed when significant clinical change occurs. Moderate evidence supports the effectiveness of multi-component interventions in increasing advance directives. Research shows that skilled facilitators and a system focusing on various key decision makers, such as patients, caregivers, and providers, as well as improving shared understanding of values are critical in the planning of care.

From the American College of Physicians, Philadelphia, Pennsylvania; Veterans Affairs Greater Los Angeles Healthcare System and RAND, Santa Monica, California; Atlantic Health, Morristown, New Jersey; Medstudy, Colorado Springs, Colorado; and Veterans Affairs Palo Alto Health Care System and Stanford University, Stanford, California.

Note: Clinical practice guidelines are guides only and may not apply to all patients and all clinical situations. Thus, they are not intended to override clinicians' judgment. All ACP clinical practice guidelines are considered automatically withdrawn or invalid 5 years after publication or once an update has been issued.

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Requests for Single Reprints: Amir Qaseem, MD, PhD, MHA, American College of Physicians, 190 N. Independence Mall West, Philadelphia, PA 19106; e-mail, aqaseem@acponline.org.

Current author addresses are available at www.annals.org.

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Current Author Addresses: Drs. Qaseem and Snow: American College of Physicians, 190 N. Independence Mall West, Philadelphia, PA 19106.
Dr. Shekelle: 1776 Main Street, Santa Monica, CA 90401.
Dr. Casey: 475 South Street, PO Box 1905, Morristown, NJ 07962.
Dr. Cross: 1761 South 8th Street, Suite H, Colorado Springs, CO 80906.
Dr. Owens: 117 Encina Commons, Stanford, CA 94305.