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.)


For author affiliations, see end of text.

*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. Doman, MD; Mary Ann Forciea, 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.
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-
IMPORTANT ELEMENTS FOR ADVANCE CARE PLANNING

Research shows that individuals are more likely to use advance directives in the presence of extensive multicomponent 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 includes 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 cardiopulmonary disease at the end of life. Clinicians should consider the use of oxygen for hypoxemia for advanced chronic obstructive pulmonary disease. Evidence also supports 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.
Disclaimer: The authors of this article are responsible for its contents, including any clinical or treatment recommendations. No statement in this article should be construed as an official position of the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

Grant Support: Financial support for the development of this guideline comes exclusively from the ACP operating budget.

Potential Financial Conflicts of Interest: Grants received: V. Snow (Agency for Healthcare Research and Quality, Centers for Disease Control and Prevention, Novo Nordisk, Pfizer, Merck & Co., Bristol-Myers Squibb, Atlantic Philanthropies, sanofi pasteur).

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.

References
5. Steinhauser KE, Christakis NA, Clipp EC, Meckley M, McIntyre L, Tulsiy JA. Factors considered important at the end of life by patients, families, physicians, and other care providers. JAMA. 2000;284:2476-82. [PMID: 11074777]
35. Windham BG, Bennett RG, Gottlieb S. Care management interventions for...


**READERS’ COMMENTS**

Readers wishing to comment on published articles should use the “Send comment/rapid response letter” option at www.annals.org. While this service is free to *Annals* subscribers, readers without subscriptions who wish to comment on articles may purchase temporary access.
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.