



# Early palliative care in cancer treatment: rationale, evidence and clinical implications

Lynn Howie and Jeffrey Peppercorn

*Ther Adv Med Oncol*

[2013] 5(6) 318–323

DOI: 10.1177/  
1758834013500375

© The Author(s), 2013.

Reprints and permissions:  
[http://www.sagepub.co.uk/  
journalsPermissions.nav](http://www.sagepub.co.uk/journalsPermissions.nav)

**Abstract:** Patients with advanced cancer often experience symptoms of disease and treatment that contribute to distress and diminish their quality of life (QOL). Care that is aimed at control of these symptoms, whether or not the patient is undergoing ongoing disease-directed therapy to control the cancer, is thus a key feature of high-quality patient-centered care. In standard oncology practice, it is easy for focus on this type of care to be obscured by discussions and management of anticancer therapy and adequate attention to QOL, patient preferences, and goals of care often occur only days to weeks from the patient's death. The initiation of palliative care and discussion of the patients' goals and preferences earlier in the course of disease can lead to improved symptom control, reduced distress throughout the disease-directed therapy, and care delivery that matches the patients' preferences. This review discusses the evolving evidence for early initiation of palliative care in patients with advanced cancer and ongoing barriers to care in this setting. We highlight challenges for research and care delivery and the potential for broader awareness of the demonstrated benefits of palliative care to help translate known benefits into improved outcomes for patients facing advanced cancer.

**Keywords:** cancer, outcomes, palliative care, treatment

## Introduction

Cancer is the second leading cause of death in the USA and accounts for one in four patient deaths annually [American Cancer Society, 2013]. Patients who present with advanced, metastatic disease can have disease control for a period of time with chemotherapy and other disease-directed interventions. However, the duration of disease control is variable, and most patients develop progression of their cancer that leads to their death within weeks, months or years. Patients with advanced cancer often have significant symptom burden, including dyspnea, pain, nausea and fatigue that can cause distress and decreased quality of life (QOL). Care that is aimed at control of symptoms whether from the cancer itself or the toxicity of treatment delivered concurrently with disease-directed therapies, is a key feature of patient-centered care [Glare, 2013; Peppercorn *et al.* 2011]. Early focus on care aimed at improving QOL has been shown to improve patient satisfaction, reduce depression and anxiety, and lead to care more consistent with patient preferences [Higginson and Evans, 2010]. In addition, early focus on such care may

improve survival and reduce overall costs of care [Connor *et al.* 2007; Morrison *et al.* 2011; Temel *et al.* 2010].

Though often thought synonymous with end-of-life care, palliative care can be defined as specialized medical care for patients with serious medical illnesses that focuses on relief from symptoms, pain, and psychological distress associated with serious illness. In standard oncology practice, discussions regarding end-of-life care and advanced symptom management often occur within days to weeks of the patient's death but the initiation of palliative care earlier in the course of disease can lead to improved symptom control and reduced distress throughout the disease-directed therapy [Keating *et al.* 2010; Mack *et al.* 2010; Wright *et al.* 2008]. In addition, these discussions result in increased referral and use of Hospice and reduced use of intensive medical care in the end-of-life setting when the disease is no longer able to be controlled [Wright *et al.* 2010].

Groups including the American Society of Clinical Oncology (ASCO), National Comprehensive

Correspondence to:

**Jeffrey Peppercorn,  
MD, MPH**

Associate Professor of  
Medicine, Duke University  
Medical Center, Durham,  
NC 27710, USA

[jeffrey.peppercorn@  
duke.edu](mailto:jeffrey.peppercorn@duke.edu)

**Lynn Howie, MD**

Duke Cancer Institute,  
Durham, NC, USA

Cancer Network and European Society of Medical Oncology have issued clinical opinions recommending the use of palliative care earlier in the course of disease based on evidence of benefit to patients or their caregivers and no evidence that early palliative care increases patient costs or causes patient or caregiver harm [Cherny *et al.* 2003; Levy *et al.* 2012; Smith *et al.* 2012]. This review discusses the evidence supporting these recommendations, how this information might translate into clinical practice, and directions for future research.

### Communication of prognosis

One of the goals of integrating palliative care earlier in the course of the disease is an effort to improve on early communication of patient prognosis in the setting of life-limiting illness. Having realistic discussions earlier in the course of disease has been shown to reduce aggressive end-of-life care and improve psychosocial well-being among patients and families [Wright *et al.* 2008]. These discussions can inform and influence patient choices for care over the course of illness.

The need to discuss disease prognosis and goals of treatment is demonstrated by studies showing that patients often overestimate their prognosis and are not clearly aware of the intent of their cancer therapy [Weeks *et al.* 2012]. It has been demonstrated that patients' preferences regarding aggressive end-of-life care (i.e. do you wish to be kept alive with a ventilator or to undergo attempts at cardiopulmonary resuscitation when you are dying?) are influenced by their understanding of their prognosis [Mack *et al.* 2012; Weeks *et al.* 1998]. Early discussions regarding prognosis influence patient choices regarding treatment throughout the course of illness and at the end of life. Furthermore these discussions allow for a better understanding of the patient's wishes by the physician. Patients who are well informed of their prognosis and given the opportunity to express their preferences for care are more likely to receive the components of care (late line chemotherapy, intensive care unit care, ventilator care, or aggressive focus on symptom management alone) that best match their preferences as reported by the patient or their caregivers [Mack *et al.* 2010]. In addition, such communication is shown to lead to less distress at the end of life for patients and their caregivers [Wright *et al.* 2008].

There is concern that frank discussion of patient prognosis could reduce patient hope and cause patient distress. However, studies have demonstrated that hope is not diminished after such discussions occur, even when bad news is delivered [Mack *et al.* 2007; Smith *et al.* 2010]. Realistic discussion of patient prognosis early in the disease course then allows for better understanding and increased awareness of the seriousness of the illness at a time when emergent decisions regarding end-of-life care are not required, which allows for patients to determine preferences regarding their treatment and care given their understanding of prognosis, and can lead to less intensive medical care at the end of life.

### Evidence for early palliative care: involvement of palliative care teams

In addition to studies focusing on early discussion of prognosis between physician and patient, studies of specialty palliative care have demonstrated an impact on patient satisfaction and QOL, use of services and costs for end-of-life care. Trials have evaluated palliative care services in inpatient and outpatient settings, and have identified benefits as well as limitations of these interventions.

In a randomized controlled trial of in-home palliative care compared with standard care, Brumley and colleagues found that participants randomized to the in-home palliative care arm were more satisfied with care at 30 and 90 days after enrollment than their usual care counterparts. Additionally, 26% of participants in the intervention arm used emergency department services compared with 33% of those in the usual care arm ( $p = 0.01$ ). Thirty-six percent of participants in the palliative care arm were hospitalized during their time in the study compared with 59% of those receiving standard care ( $p < 0.001$ ). These differences, which were shown not to be attributable to differences in follow up, resulted in an average of around 4 fewer days in hospital and 35% fewer emergency room visits for patients receiving home palliative care [Brumley *et al.* 2007].

Rabow and colleagues randomly assigned outpatients with chronic illness with a life expectancy of 1–5 years to usual care *versus* usual care plus involvement of a comprehensive palliative care team (CCT) which consisted of physicians, a nurse, social worker, chaplain, pharmacist, psychologist, art therapist and volunteer coordinator.

Thirty-three percent of the participants carried a cancer diagnosis. There was a range of interventions, including classes, support groups, visits and telephone calls. Participants in the CCT arm reported less dyspnea, anxiety and improved sleep quality and spiritual wellbeing, however had no change in pain, depression or QOL. Part of the lack of improvement in pain and depression may be explained by the lack of implementation of CCT recommendations by the primary care physician. This study additionally demonstrated fewer primary care and urgent care visits by participants in the intervention arm without an increase in emergency room visits, hospitalizations or number of days in the hospital. This study demonstrated improvement in some symptoms but also demonstrated some of the challenges of implementing comprehensive palliative care, including the issue of communication between the palliative care team and the primary care providers. For example, in this study, a great majority (91%) of patients had no documentation of implementation of palliative care recommendations for pain management. Barriers to implementation of palliative care recommendations must be better understood or we may continue to underestimate the potential impact these interventions could have on patient outcomes [Rabow *et al.* 2004].

The benefits of inpatient specialty palliative care teams for patient satisfaction and healthcare utilization have also been demonstrated. Gade and colleagues demonstrated in a multicenter randomized controlled trial of participants in an integrated health plan that inpatient palliative care services (ICPS) composed of physicians, nurses, social workers and chaplains improved patient satisfaction, led to increased duration of hospice care and fewer intensive care unit admissions among those who were randomized to the ICPS intervention [Gade *et al.* 2008]. However, demonstration of improvement in patient symptoms as a result of receipt of these services has been less clear. Pantilat and colleagues randomized patients with chronic illness to receive an inpatient palliative medicine consultation *versus* standard disease management. All participants in this study had improvements in symptoms over the course of time, including pain, dyspnea and anxiety. There was no significant difference in symptom improvement between participants receiving the intervention *versus* standard care. As seen in previous studies, there were issues regarding implementation of palliative care recommendations. It is

possible that the benefits of specialized palliative care involvement may be confined to a subset of patients with specific needs or symptom burden that must be identified in further studies [Pantilat *et al.* 2010]. However, adherence to treatment recommendations was low, thus it is possible that the lack of differences between arms may be due to barriers to implementation of palliative care recommendations as opposed to the impact of the recommended interventions themselves. This issue clearly requires elucidation and further study.

### Evidence for early palliative care in lung cancer

A pivotal 2010 study by Temel and colleagues demonstrated the benefit of early palliative care in patients newly diagnosed with metastatic non-small cell lung cancer. In this study, participants were randomized to standard oncological care *versus* standard care integrated with palliative care (EPC) at the time of diagnosis. Those randomized to the EPC arm had visits with a palliative care team consisting of board-certified physicians and nurse practitioners within 3 weeks of study enrollment and were followed at least monthly along with standard oncologic care. The focus of the palliative care intervention was attention to symptoms and goals of care. Patients assigned to the standard oncological care arm did not receive evaluations by palliative care physicians unless requested by the patient, family or provider.

Patient outcomes were evaluated using the Functional Assessment of Cancer Therapy – Lung (FACT-L), the Lung Cancer Subscale (LCS) and the Trial Outcome Index (TOI) to assess QOL, and the Health and Depression Scale, and Patient Health Questionnaire 9 survey were used to assess participant mood. Healthcare utilization was also measured. After 12 weeks, participants randomized to the EPC group had statistically significant differences in the three measures of QOL (FACT-L score 98 EPC, 91.5 SC,  $p = 0.03$ ; LCS score 21.0 EPC *versus* 19.3 SC,  $p = 0.04$ ; and TOI score 59.0 EPC *versus* 53.0 SC,  $p = 0.009$ ). Participants in the palliative care arm reported fewer depressive symptoms than participants who received standard oncological care. In addition to improved QOL and decreased symptoms, participants in the early palliative care arm were less likely to receive aggressive end-of-life care (33% *versus* 54%,  $p = 0.05$ ) and were more likely to have their preferences regarding resuscitation

documented in the medical record (53% *versus* 28%,  $p = 0.05$ ).

A provocative finding of this study was that patients in the EPC arm lived longer than their counterparts receiving standard care. Though participants in the early palliative care arm received less aggressive care at the end of life, the median survival of participants in this arm of the study was 11.6 months compared with 8.9 months for those who received standard care ( $p = 0.02$ ). While this was not a primary endpoint, this result suggests that early palliative care may help to control symptoms and improve QOL which then translate into a survival advantage without the use of aggressive medical care. This important finding suggests to physicians and patients that a focus on palliative care need not translate into 'giving up' or a focus on QOL alone, as some fear, and may prolong survival while also achieving other goals of care.

This study demonstrated the benefit of early palliative care in patients with metastatic non-small cell lung cancer. Participants were recruited within a short period from diagnosis and, for those in the EPC arm, this meant involvement of the palliative care team before symptoms were out of control or when the end of life was imminent. Though a valuable study, it should be noted that it may have limited generalizability as it was performed at a single academic medical center and enrolled patients with a single diagnosis. There was not an attention control arm to help demonstrate that the palliative care intervention was effective for its content rather than for the additional time and attention (which might be delivered with fewer resources) directed towards the participant aside from standard oncologic care. While there were general guidelines for the intervention, there was latitude within the palliative care intervention to allow for individualization of the intervention to address symptoms, psychosocial issues, and goals of care. This allowed for greater individualization of the intervention, but it complicates determination of which portions of the intervention were most effective. However, community-based palliative care consisting of outpatient specialty trained palliative care physicians, nurses and social workers is not available as standard in clinical practice for patients receiving active therapy, and so better understanding the components of the intervention that were most helpful is critical to achieve the benefits seen in this study on a wider scale.

### Implications for clinical practice

How early to involve palliative care in the care of patients with cancer is subject to debate. The ASCO provisional clinical opinion recommends introduction of palliative care at the time of diagnosis for patients with metastatic lung cancer based on the result of the Temel study, demonstrating evidence of benefit. In other disease types, there is more variability in survival even in the setting of metastatic disease. Provisional recommendations have been made to offer palliative care at the diagnosis of metastatic disease or in patients who have a significant symptom burden. Yet for patients with advanced disease experiencing significant symptom burden from anxiety, depression and other forms of distress, it is not clear that specialized involvement of a palliative care team or physician is always needed or most effective compared with existing treatment through psychosocial support programs. Defining the ideal time of palliative care intervention (and components of that intervention) is likely going to be somewhat disease and even patient specific. Identification of patients in whom symptom burden is high will require careful evaluation by the primary oncologist and is likely to maximize the benefits of palliative care. Additionally, studies of interventions in other metastatic disease settings (including common cancers such as breast and prostate) will be important to validate benefits of early intervention in other settings, to clarify the components of palliative care that are required to improve outcomes and determine whether the improvements in survival in the Temel study can be demonstrated across various disease types. Given the demonstrated potential of palliative care and the reality of constrained resources and difficulty at scaling some of the interventions studied to date to the broad population of patients with advanced cancer, such research is urgently required.

Determining who delivers this care is an important step in establishing delivery of early palliative care services for these patients. The trials discussed in this review had specialty trained palliative care providers delivering the intervention. However, demand exceeds supply of these specialty providers and current systems of reimbursement often do not compensate this type of care along with disease-directed therapies. Given this, it has been recommended that oncologists have additional training in communication as well as symptom management to be able to provide standard palliative treatments for their patients



[Quill and Abernethy, 2013]. Oncologists with this training may have ongoing discussions with their patients from the diagnosis of metastatic disease which lead to less use of third- and fourth-line therapies which are less effective and may be more toxic, and may ease the transition from cancer-directed therapies to palliative therapies for their patients with advance illness [Shanafelt *et al.* 2004]. Additional training in discussion of realistic expectations of continued aggressive care *versus* a transition of care to that focused on reduction of symptom burden may be what is most needed to improve patient outcomes. However, whether this does lead to measurable differences in patient outcomes is yet to be evaluated.

### Directions for the future

Additional research is necessary to further understand the role of early palliative care in various cancer types as well as various cancer stages. Further studies using multiple centers including a greater diversity of patient populations to better understand how patient characteristics affect the potential benefit of these services are needed. Trials that control for patients' exposure to attention from the intervention and that evaluate other specific components of palliative care will better elucidate which portions of a palliative care intervention might be most helpful for patients. Furthermore, comparisons of similar services by oncologists who have received additional palliative care training compared with palliative care specialists will help to identify whether integration of these services by primary oncologists is as effective as management of consultation by palliative care teams. Critical workforce issues loom on the horizon and research is needed to help determine what specific services and what specific service providers are needed to optimally and sustainably deliver palliative care in a scalable fashion that may benefit patients with cancer in the USA, other high-resource countries and in the developing world.

The evidence base to support early palliative care is beginning to accumulate. It is clear that early discussions regarding disease prognosis are a crucial first step in helping patients to better understand their treatment choices and goals of care. For many patients with advanced cancer, it is likely that early involvement of palliative care will improve outcomes, including QOL, and potentially survival. Further research and greater awareness of the demonstrated benefits

of palliative care will help us translate the benefits of palliative care to more patients facing advanced cancer.

### Funding

This work was supported by the Greenwall Foundation for Bioethics.

### Conflict of interest statement

The authors declare no conflict of interest in preparing this article.

### References

- American Cancer Society (2013) *Cancer Facts & Figures*. <http://www.cancer.org/research/cancerfactsfigures/cancerfactsfigures/cancer-facts-figures-2013> (accessed 23 July 2013).
- Brumley, R., Enguidanos, S., Jamison, P., Seitz, R., Morgenstern, N., Saito, S. *et al.* (2007) Increased satisfaction with care and lower costs: results of a randomized trial of in-home palliative care. *J Am Geriatr Soc* 55: 993–1000.
- Cherny, N., Catane, R., Kosmidis, P., Supportive, E. and Palliative, C. (2003) ESMO takes a stand on supportive and palliative care. *Ann Oncol* 14: 1335–1337.
- Connor, S., Pyenson, B., Fitch, K., Spence, C. and Iwasaki, K. (2007) Comparing hospice and nonhospice patient survival among patients who die within a three-year window. *J Pain Symptom Manage* 33: 238–246.
- Gade, G., Venohr, I., Conner, D., McGrady, K., Beane, J., Richardson, R. *et al.* (2008) Impact of an inpatient palliative care team: a randomized control trial. *J Palliat Med* 11: 180–190.
- Glare, P. (2013) Early implementation of palliative care can improve patient outcomes. *J Natl Compr Canc Netw* 11(Suppl. 1): S3–S9.
- Higginson, I. and Evans, C. (2010) What is the evidence that palliative care teams improve outcomes for cancer patients and their families? *Cancer J* 16: 423–435.
- Keating, N., Beth Landrum, M., Arora, N., Malin, J., Ganz, P., van Ryn, M. *et al.* (2010) Cancer patients' roles in treatment decisions: do characteristics of the decision influence roles? *J Clin Oncol* 28: 4364–4370.
- Levy, M., Adolph, M., Back, A., Block, S., Codada, S., Dalal, S. *et al.* (2012) Palliative care. *J Natl Compr Canc Netw* 10: 1284–1309.
- Mack, J., Cronin, A., Keating, N., Taback, N., Huskamp, H., Malin, J. *et al.* (2012) Associations

- between end-of-life discussion characteristics and care received near death: a prospective cohort study. *J Clin Oncol* 30: 4387–4395.
- Mack, J., Weeks, J., Wright, A., Block, S. and Prigerson, H. (2010) End-of-life discussions, goal attainment, and distress at the end of life: predictors and outcomes of receipt of care consistent with preferences. *J Clin Oncol* 28: 1203–1208.
- Mack, J., Wolfe, J., Cook, E., Grier, H., Cleary, P. and Weeks, J. (2007) Hope and prognostic disclosure. *J Clin Oncol* 25: 5636–5642.
- Morrison, R., Dietrich, J., Ladwig, S., Quill, T., Sacco, J., Tangeman, J. *et al.* (2011) Palliative care consultation teams cut hospital costs for Medicaid beneficiaries. *Health Aff (Millwood)* 30: 454–463.
- Pantilat, S., O’Riordan, D., Dibble, S. and Landefeld, C. (2010) Hospital-based palliative medicine consultation: a randomized controlled trial. *Arch Intern Med* 170: 2038–2040.
- Peppercorn, J., Smith, T., Helft, P., Debono, D., Berry, S., Wollins, D. *et al.* (2011) American society of clinical oncology statement: toward individualized care for patients with advanced cancer. *J Clin Oncol* 29: 755–760.
- Quill, T. and Abernethy, A. (2013) Generalist plus specialist palliative care – creating a more sustainable model. *N Engl J Med* 368: 1173–1175.
- Rabow, M., Dibble, S., Pantilat, S. and McPhee, S. (2004) The comprehensive care team: a controlled trial of outpatient palliative medicine consultation. *Arch Intern Med* 164: 83–91.
- Shanafelt, T., Loprinzi, C., Marks, R., Novotny, P. and Sloan, J. (2004) Are chemotherapy response rates related to treatment-induced survival prolongations in patients with advanced cancer? *J Clin Oncol* 22: 1966–1974.
- Smith, T., Dow, L., Virago, E., Khatcheressian, J., Lyckholm, L. and Matsuyama, R. (2010) Giving honest information to patients with advanced cancer maintains hope. *Oncology* 24: 521–525.
- Smith, T., Temin, S., Alesi, E., Abernethy, A., Balboni, T., Basch, E. *et al.* (2012) American Society of Clinical Oncology provisional clinical opinion: the integration of palliative care into standard oncology care. *J Clin Oncol* 30: 880–887.
- Temel, J., Greer, J., Muzikansky, A., Gallagher, E., Admane, S., Jackson, V. *et al.* (2010) Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med* 363: 733–742.
- Weeks, J., Catalano, P., Cronin, A., Finkelman, M., Mack, J., Keating, N. *et al.* (2012) Patients’ expectations about effects of chemotherapy for advanced cancer. *N Engl J Med* 367: 1616–1625.
- Weeks, J., Cook, E., O’Day, S., Peterson, L., Wenger, N., Reding, D. *et al.* (1998) Relationship between cancer patients’ predictions of prognosis and their treatment preferences. *JAMA* 279: 1709–1714.
- Wright, A., Mack, J., Kritek, P., Balboni, T., Massaro, A., Matulonis, U. *et al.* (2010) Influence of patients’ preferences and treatment site on cancer patients’ end-of-life care. *Cancer* 116: 4656–4663.
- Wright, A., Zhang, B., Ray, A., Mack, J., Trice, E., Balboni, T. *et al.* (2008) Associations between end-of-life discussions, patient mental health, medical care near death, and caregiver bereavement adjustment. *JAMA* 300: 1665–1673.

Visit SAGE journals online  
<http://tam.sagepub.com>

 SAGE journals