



Published in final edited form as:

*Palliat Med.* 2018 April ; 32(4): 757–766. doi:10.1177/0269216317751893.

## Differential Effects of Early Palliative Care based on the Age and Sex of Patients with Advanced Cancer from a Randomized Controlled Trial

Ryan D. Nipp, M.D.<sup>a</sup>, Areej El-Jawahri, M.D.<sup>a</sup>, Lara Traeger, Ph.D.<sup>b</sup>, Jamie M. Jacobs, Ph.D.<sup>b</sup>, Emily R. Gallagher, R.N.<sup>a</sup>, Elyse R. Park, Ph.D., M.P.H.<sup>b</sup>, Vicki A. Jackson, M.D., M.P.H.<sup>c</sup>, William F. Pirl, M.D., M.P.H.<sup>d</sup>, Jennifer S. Temel, M.D.<sup>a</sup>, and Joseph A. Greer, Ph.D.<sup>b</sup>

<sup>a</sup> Department of Medicine, Division of Hematology & Oncology, Massachusetts General Hospital Cancer Center & Harvard Medical School, Boston, Massachusetts, USA;

<sup>b</sup> Department of Psychiatry, Massachusetts General Hospital & Harvard Medical School, Boston, Massachusetts, USA;

<sup>c</sup> Department of Medicine, Division of Palliative Care, Massachusetts General Hospital & Harvard Medical School, Boston, Massachusetts, USA

<sup>d</sup> Department of Psychiatry, Sylvester Comprehensive Cancer Center & University of Miami, Miami, Florida, USA

### Abstract

**Background:** Early palliative care (EPC) interventions enhance patient outcomes including quality of life (QOL), mood, and coping, but it remains unclear whether certain subgroups of patients are more likely to benefit from EPC. We explored whether age and sex moderate the improved outcomes seen with EPC.

**Methods:** We performed a secondary analysis of data from a randomized trial of 350 patients with advanced lung and non-colorectal gastrointestinal cancer. Patients received an EPC intervention integrated with oncology care or usual oncology care alone. We used linear regression to determine if age (older or younger than 65) and sex moderated the effects of the intervention on QOL (Functional Assessment of Cancer Therapy-General [FACT-G]), depression symptoms (Patient Health Questionnaire 9 [PHQ-9]), and coping (Brief COPE) within lung and gastrointestinal subgroups.

**Results:** At 24-weeks, younger patients with lung cancer receiving EPC reported increased use of active coping ( $B=1.74$ ;  $P=0.02$ ) and decreased use of avoidant coping ( $B=-0.97$ ;  $P=0.02$ ), but

---

**Address Correspondence:** Dr. Ryan Nipp at Massachusetts General Hospital, 55 Fruit St., Yawkey, Boston, MA 02114, RNipp@MGH.harvard.edu, P: 617-724-4000, F: 617-724-1135.

**Author Contributions:** All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data. All were involved in drafting the article or revising it critically for important intellectual content. All provided final approval of the manuscript and agree to be accountable for all aspects of the work.

**Conflict of Interest Disclosures:** Ryan Nipp, Areej El-Jawahri, Lara Traeger, Jamie Jacobs, Emily Gallagher, Elyse Park, Vicki Jackson, William Pirl, Jennifer Temel, and Joseph Greer have no conflicts of interest to disclose.

**Ethics and Consent:** The Dana-Farber Cancer Institute/Harvard Cancer Center Institutional Review Board approved the study protocol, and all patients provided written informed consent.

the effects of EPC on these outcomes were not significant for older patients. Male patients with lung cancer assigned to EPC reported better QOL (FACT-G: B=9.31; P=0.01) and lower depression scores (PHQ-9: B=-2.82; P=0.02), but the effects of EPC on these outcomes were not significant for female patients. At 24-weeks, we found no age or sex moderation effects within the gastrointestinal cancer subgroup.

**Conclusion:** Age and sex moderate the effects of EPC for patients with advanced lung cancer. EPC may need to be tailored to individuals' unique sociodemographic and clinical characteristics.

## Keywords

palliative care; quality of life; depression symptoms; coping; advanced cancer; geriatrics

## Introduction:

Early integration of palliative care with oncology care often benefits patients with cancer. Studies demonstrate that patients with advanced cancer who receive early palliative care experience improved quality of life (QOL), mood, and coping.<sup>1-6</sup> Based on this evidence, the American Society of Clinical Oncology (ASCO) recommends the involvement of palliative care early in the course of illness for patients with advanced cancer or high symptom burden.<sup>7, 8</sup> Thus, the demand for palliative care services continues to rise.<sup>9-14</sup> However, minimal research is available to clarify whether certain subgroups of patients are more or less likely to experience the benefits of early palliative care. We therefore lack data regarding how best to tailor the integrated palliative care model to each individual's unique care needs.

Patients' palliative care needs likely differ according to their unique sociodemographic and clinical characteristics. In prior work, we demonstrated that patients' demographic factors, such as age and sex, moderated the improvements in QOL and mood seen with early palliative care.<sup>15</sup> Specifically, we found that males and younger patients who received early palliative care experienced better QOL and mood than those assigned to usual oncology care alone, yet these outcomes did not differ significantly between treatment groups for females or older patients. However, this study involved only patients with advanced non-small cell lung cancer, and we lacked information about other important outcomes, such as patients' use of coping strategies. Notably, patients' use of certain coping strategies differs by age and sex.<sup>16-19</sup> Moreover, a recent study of early palliative care in patients with advanced lung and gastrointestinal cancer demonstrated differential effects by cancer type.<sup>20</sup> Thus, while data suggest that the benefits of palliative care may differ according to patients' distinct clinical and sociodemographic characteristics, additional research is needed to define the differential effects of palliative care models in order to inform efforts to provide palliative care services personalized to the unique needs of each patient with cancer.

In the current study, we sought to corroborate and expand upon prior findings by exploring whether age and sex moderate the effects of palliative care on QOL, depression symptoms, and coping strategies among patients with advanced lung and gastrointestinal malignancies participating in a randomized trial of early palliative care. Specifically, we hypothesized, based on our prior work, that the benefits of early palliative care would be greater for males

and younger patients.<sup>15</sup> By studying the differential effects of early palliative care based on patients' age and sex, we hope to better understand how these factors modify both their cancer experience and palliative care needs. Findings from this work will aid in the development of strategies to tailor care to the specific palliative care concerns of patients with cancer and establish a framework for personalized palliative care.

## Methods:

### Study Design

We conducted a secondary, exploratory analysis of data collected from a randomized trial of early palliative care integrated with oncology care compared with usual oncology care.<sup>20</sup> The study procedures have been previously described, but briefly, we randomly assigned patients in a 1:1 fashion with newly diagnosed, incurable lung or non-colorectal gastrointestinal malignancies to receive early palliative care integrated with oncology care or oncology care alone. Patients assigned to early palliative care met with a member of the outpatient palliative care team, which consisted of board-certified palliative care physicians and advanced-practice nurses, within four weeks after enrollment and at least monthly thereafter until death. Patients assigned to usual oncology care were not referred to palliative care unless requested by the patient, family, or oncologist. The Dana-Farber/Harvard Cancer Care institutional review board approved the study protocol.

### Patient Selection

In the parent trial, we enrolled 350 patients with newly diagnosed (within the previous eight weeks) incurable lung or non-colorectal gastrointestinal cancer presenting to Massachusetts General Hospital (MGH) from May 2011 to July 2015. Patients were also required to receive their care at MGH, be at least 18 years of age, have no history of therapy for metastatic disease, have an Eastern Cooperative Oncology Group performance status of 0 to 2, and be able to read and respond to questions in English or complete questionnaires with minimal assistance from an interpreter. We excluded patients already receiving palliative care services, those needing immediate referral for palliative care or hospice, and those with significant psychiatric or other comorbid disease prohibiting participation.

### Study Measures

**Data Collection**—Study participants completed a demographic questionnaire and baseline self-report measures following written, informed consent and prior to random assignment. We conducted follow-up assessments 24 weeks following enrollment (or within 3 weeks of this time point). Participants self-reported their race, ethnicity, religion, relationship status, education, presence of dependent children, and annual income. We reviewed electronic health records to obtain participants' age, sex, Eastern Cooperative Oncology Group performance status, and cancer diagnosis, stage, and therapy.

**Quality of Life**—We evaluated patients' QOL using the Functional Assessment of Cancer Therapy-General (FACT-G), which has been validated for use in multiple care settings and with diverse tumor types.<sup>21</sup> The FACT-G assesses patients' well-being across four domains

(physical, functional, emotional, and social) during the prior seven days, with higher scores indicating better QOL.

**Depression Symptoms**—We assessed patients' mood symptoms using the Patient Health Questionnaire 9 (PHQ-9).<sup>22</sup> The PHQ-9 is a nine-item measure that evaluates symptoms of major depressive disorder according to criteria from the Diagnostic and Statistical Manual of Mental Disorders-IV, with higher scores indicating worse depression symptoms.

**Coping Strategies**—We used the Brief COPE to assess patients' use of coping strategies. The Brief COPE is a 28-item questionnaire that assesses 14 coping strategies using two items for each strategy.<sup>23</sup> To minimize questionnaire burden for participants, we limited our assessment to the following seven coping strategies (i.e., 14 items), which we felt were most appropriate for our study population: emotional support, positive reframing, active, acceptance, self-blame, denial, and behavioral disengagement. Consistent with recommendations to create higher-order factors from among the coping strategies assessed using the Brief COPE,<sup>24</sup> we conducted a higher-order factor analysis, and this revealed a two-factor solution, which we used previously.<sup>6, 25</sup> One of the higher-order factors included active coping, positive reframing, and acceptance, which we labeled "active coping" since these strategies actively engage in addressing the problem. The second higher-order factor consisted of denial and self-blame, which we refer to as "avoidant coping." Higher scores on each factor indicate greater use of those strategies.

## Statistical Analysis

We used descriptive statistics to describe patient demographics and study variables. Based on prior work demonstrating a differential effect of early palliative care based on cancer type,<sup>20</sup> we compared baseline differences between patients with lung and gastrointestinal cancer and performed all moderation analyses within these separate cancer type subgroups. In addition, we used an age cutoff of 65 years for age subgroup analyses, consistent with prior research.<sup>26–29</sup> To assess the degree to which patients' age and sex moderated the effects of early palliative care on QOL (FACT-G), depressive symptoms (PHQ-9), and coping strategies (Brief COPE) at week 24, we computed separate linear regression models for each outcome that included the following independent variables: baseline criterion scores, group assignment, the moderating variable (age or sex), and an interaction term between group assignment and the moderating variable. We considered interaction terms with  $p < 0.15$  to indicate potential moderation worth exploring subsequent subgroup differences.<sup>30, 31</sup> Specifically, we then used linear regression to determine the effects of early palliative care on QOL, depression symptoms, and coping strategies within the subgroups of age and sex. To help illustrate these findings, we compared week 24 QOL, depression symptoms, and coping strategies between study groups by age and sex using independent-samples Student's *t*-tests. We used SPSS version 20 for statistical analyses.

## Results:

### Participant Sample

Of 480 eligible patients, 350 (72.9%) enrolled in the study. We found no significant differences in the age, sex, or cancer type of the patients enrolled in the study versus those not enrolled (Supplemental Table 1). Patients offered the study who refused study enrollment most often cited that they were ‘not interested in the study’ (50.4%). As shown in Table 1, just over half had a diagnosis of lung cancer (54.6%), were age 65 (51.7%), and male (54.0%). Compared to those with gastrointestinal cancer, patients with lung cancer were more likely to be female (52.9% vs 37.7%,  $p=0.005$ ), have a smoking history 10 pack years (72.3% vs 31.4%,  $p<0.001$ ), and an education level of high school and below (42.4% vs 31.4%,  $p=0.036$ ). We did not find a significant difference in the proportion of male or female participants in the older or younger subgroups (Supplemental Table 2).

### Outcomes by Patients’ Age

Using linear regression, we found that patients’ age did not moderate the effects of early palliative care on QOL and depression symptoms. However, patients’ age did moderate the effect of early palliative care on use of avoidant coping strategies (age $\times$ group assignment, unstandardized coefficient [B]:0.98, standard error [SE]=0.58, 95% confidence interval [CI]=−0.18 to 2.13,  $p=0.097$ ) among patients with lung cancer. Specifically, subsequent subgroup analyses by age (Table 2) showed that, among younger patients with lung cancer (i.e., age <65 years), early palliative care decreased the use of avoidant coping (B:−0.97, SE=0.41, 95%CI:−1.78 to −0.16,  $p=0.020$ ) but had no effect on this outcome for older patients with lung cancer. As illustrated in Figure 1, the use of avoidant coping decreased from baseline to week 24 for both younger and older patients with lung cancer, whereas those assigned to usual oncology care had relatively stable use of avoidant coping over time. Notably, the differences in use of coping strategies between those assigned to early palliative care versus usual oncology care only reached statistical significance among the younger patients with lung cancer. Moreover, we found that the avoidant coping outcome was not normally distributed, and therefore we ran sensitivity analyses with log transformed data, which confirmed our findings.

In addition, although we did not observe a significant moderation effect by age on active coping strategies, subsequent subgroup analyses revealed that early palliative care also led to increased use of active coping (B:1.74, SE=0.74, 95%CI:0.26 to 3.23,  $p=0.022$ ) among younger patients with lung cancer. This relationship did not reach the threshold for statistical significance in older patients. Figure 1 illustrates that the use of active coping increased from baseline to week 24 for the younger and older patients with lung cancer assigned to early palliative care, but use of active coping decreased during this time for both younger and older patients assigned to usual oncology care. Finally, we found no other significant moderation effects of early palliative care by patient age in either the lung or gastrointestinal cancer groups.

## Outcomes by Patients' Sex

Using linear regression, we found that patients' sex moderated the effects of early palliative care on QOL (sex $\times$ group assignment, B:−8.61, SE=4.90, 95%CI:−18.31 to 1.10, p=0.082) and depression symptoms (sex $\times$ group assignment, B:2.89, SE=1.64, 95%CI:−0.35 to 6.14, p=0.080) for patients with lung cancer. However, patients' sex did not moderate the effect of early palliative care on use of avoidant or active coping strategies. In subsequent subgroup analyses by sex (Table 3), we found that, among male patients with lung cancer, early palliative care resulted in improved QOL (B:9.31, SE=3.66, 95%CI:1.98 to 16.65, p=0.014) and lower depression symptom scores (B:−2.82, SE=1.13, 95%CI:−5.08 to −0.55, p=0.016). However, early palliative care did not have significant effects on the QOL and mood of female patients. We found no significant moderation effects of early palliative care by sex among patients with gastrointestinal cancer.

As illustrated in Figure 2, QOL increased from baseline to week 24 for male patients with lung cancer assigned to early palliative care, yet the QOL for males with lung cancer assigned to usual oncology care decreased from baseline to week 24. Notably, female patients with lung cancer experienced improved QOL regardless of their treatment group assignment. Similarly, Figure 2 also illustrates that male patients with lung cancer assigned to early palliative care experienced decreased depression symptom scores from baseline to week 24, whereas those assigned to usual oncology care had increased depression symptom scores over time. Again, female patients with lung cancer in both the early palliative care and usual oncology care arms experienced reduced depression symptom scores over time.

## Discussion:

In this secondary, exploratory analysis of data from a randomized trial assessing the impact of early palliative care among patients with advanced lung and gastrointestinal cancer, we found that age and sex moderated some of the benefits derived from early palliative care. We demonstrated that patients' age moderated the effects of early palliative care on coping strategies among those with lung cancer. We also found that, among those with lung cancer, patients' sex moderated the effects of early palliative care on QOL and depression symptoms. Notably, we found no significant moderation effects on these outcomes by age or sex among patients with gastrointestinal cancer, potentially related to our prior data suggesting a lack of significant intervention effects for QOL and depression scores by 24 weeks in the gastrointestinal cancer cohort.<sup>20</sup> Collectively these findings corroborate our previous results,<sup>15</sup> and provide additional evidence demonstrating the potential differential effects of early palliative care based on patients' age and sex.

Our work highlights the importance of accounting for age and sex in future efforts to develop supportive care interventions tailored to patients' unique needs. A more comprehensive understanding about how patients' clinical and sociodemographic characteristics may relate to their palliative care needs can be informative in: (1) enhancing current models of care by providing personalized palliative care services; (2) identifying patients who may benefit most from targeted interventions; and (3) developing novel care models tailored to patients' unique care needs to improve outcomes. By demonstrating the differential effects of early palliative care based on patients' age and sex, our study



underscores the need to account for patients' unique clinical and sociodemographic factors when designing palliative care interventions and will help inform future efforts to enhance outcomes for patients with advanced cancer and better support this population with diverse care needs.

To our knowledge, this is the first study to report that the effects of palliative care on patients' coping outcomes differ according to their age. We found that early palliative care helped younger patients with lung cancer adopt more active coping strategies and utilize less avoidant coping mechanisms, but these benefits were not significant for the older patients in our study. Clinically, these findings are important, as evidence suggests that the use of active coping behavior is associated with better QOL and mood, and that patients' coping strategies may mediate the benefits of palliative care.<sup>6, 18, 32</sup> Thus, in future work, investigators should seek to understand the mechanisms underlying the improvements in coping seen for the younger patients with this early palliative care model, while also investigating novel models of care adapted to the unique needs of older adults with advanced cancer in order to enhance outcomes for these patients.<sup>33–35</sup> As the population of aging individuals continues to increase,<sup>36</sup> it is imperative that we design oncology care models targeting the unique palliative and geriatric care needs of older adults with cancer.

Importantly, we also demonstrated that patients' sex moderated the impact of early palliative care for patients with lung cancer. As with our prior study, male patients with lung cancer assigned to early palliative care experienced better QOL and mood compared with those assigned to usual oncology care, but these outcomes were not significantly different for the female patients.<sup>15</sup> Importantly, the mean QOL difference of nearly 10 points among the males at week 24 surpasses previously published cutoffs considered clinically meaningful.<sup>37, 38</sup> Also consistent with our prior work, female participants with lung cancer in both study groups experienced improvements in their QOL and mood, suggesting that female patients are resilient in having their supportive care needs addressed, both with and without palliative care involvement. Studies show that women more actively seek out and accept additional supportive care services, which may ensure they have their supportive care needs appropriately met through various mechanisms.<sup>39–41</sup> Therefore, our findings support that patients' sex qualifies their experience with early palliative care, providing further evidence of the significant benefits that early integration of palliative care can have on the QOL and mood outcomes of male patients with advanced lung cancer.

Our study has several limitations. First, this was an exploratory analysis, and prospective studies designed to test the differential effects of early palliative care across specific clinical and sociodemographic characteristics are still needed. Second, our study included a homogenous sample from a tertiary cancer center with a specialized palliative care team, limiting our ability to generalize findings to patients outside of this population and care setting. Specifically, we focused on patients with incurable lung and non-colorectal gastrointestinal malignancies and we cannot comment on whether our results would apply to patients with other cancer types. Third, the current analysis involves one specific model of palliative care, and thus the results may not apply to different care models. Finally, we are unable to account for potentially important unmeasured confounds, including functional status, social support, and cognition. We focused our current analysis on age and sex as

moderators, but future research into the differential effects of palliative care based on certain clinical and sociodemographic factors should also address whether other potentially important characteristics are associated with patients' experience with palliative care.

In summary, we demonstrated differential effects of early palliative care based on patients' age and sex. We found that younger patients with lung cancer who received early palliative care reported increased use of active coping and decreased use of avoidant coping, but these benefits were not significant for older patients. In addition, our results demonstrate that male patients with lung cancer who received early palliative care experienced improved QOL and mood, yet female patients did not experience these same significant effects. These results help corroborate findings from our previous work and further our understanding about how patients' clinical and sociodemographic factors may modify both their cancer experience and palliative care needs. Expanding on this work, future investigators may seek to develop strategies for tailoring and personalizing palliative care services to the individual supportive care needs of patients with advanced cancer.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Funding sources:

Supported by the Palliative Care Research Cooperative Group funded by National Institute of Nursing Research U24NR014637 (Nipp); NINR R01 NR012735 (Temel) and NCI K24 CA181253 (Temel)

## References

1. Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. *The New England journal of medicine*. 2010; 363: 733–42. [PubMed: 20818875]
2. Zimmermann C, Swami N, Krzyzanowska M, et al. Early palliative care for patients with advanced cancer: a cluster-randomised controlled trial. *Lancet*. 2014; 383: 1721–30. [PubMed: 24559581]
3. Temel JS, Jackson VA, Billings JA, et al. Phase II study: integrated palliative care in newly diagnosed advanced non-small-cell lung cancer patients. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2007; 25: 2377–82. [PubMed: 17557950]
4. Bakitas M, Lyons KD, Hegel MT, et al. Effects of a palliative care intervention on clinical outcomes in patients with advanced cancer: the Project ENABLE II randomized controlled trial. *JAMA : the journal of the American Medical Association*. 2009; 302: 741–9. [PubMed: 19690306]
5. Temel JS, Greer JA, Admane S, et al. Longitudinal perceptions of prognosis and goals of therapy in patients with metastatic non-small-cell lung cancer: results of a randomized study of early palliative care. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2011; 29: 2319–26. [PubMed: 21555700]
6. Greer JA, Jacobs JM, El-Jawahri A, et al. Role of Patient Coping Strategies in Understanding the Effects of Early Palliative Care on Quality of Life and Mood. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2017: JCO2017737221.
7. Smith TJ, Temin S, Alesi ER, et al. American Society of Clinical Oncology provisional clinical opinion: the integration of palliative care into standard oncology care. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2012; 30: 880–7. [PubMed: 22312101]
8. Ferrell BR, Temel JS, Temin S, et al. Integration of Palliative Care Into Standard Oncology Care: American Society of Clinical Oncology Clinical Practice Guideline Update. *Journal of clinical*



oncology : official journal of the American Society of Clinical Oncology. 2017; 35: 96–112. [PubMed: 28034065]

9. Lupu D, American Academy of H and Palliative Medicine Workforce Task F. Estimate of current hospice and palliative medicine physician workforce shortage. *Journal of pain and symptom management*. 2010; 40: 899–911. [PubMed: 21145468]
10. Quill TE and Abernethy AP. Generalist plus specialist palliative care--creating a more sustainable model. *The New England journal of medicine*. 2013; 368: 1173–5. [PubMed: 23465068]
11. Kamal AH, Bull JH, Swetz KM, Wolf SP, Shanafelt TD and Myers ER. Future of the Palliative Care Workforce: Preview to an Impending Crisis. *The American journal of medicine*. 2017; 130: 113–4. [PubMed: 27687068]
12. Morrison RS, Augustin R, Souvanna P and Meier DE. America's care of serious illness: a state-by-state report card on access to palliative care in our nation's hospitals. *Journal of palliative medicine*. 2011; 14: 1094–6. [PubMed: 21923412]
13. Hui D, Elsayem A, De la Cruz M, et al. Availability and integration of palliative care at US cancer centers. *JAMA : the journal of the American Medical Association*. 2010; 303: 1054–61. [PubMed: 20233823]
14. Rabow MW, O'Riordan DL and Pantilat SZ. A statewide survey of adult and pediatric outpatient palliative care services. *Journal of palliative medicine*. 2014; 17: 1311–6. [PubMed: 25137356]
15. Nipp RD, Greer JA, El-Jawahri A, et al. Age and Gender Moderate the Impact of Early Palliative Care in Metastatic Non-Small Cell Lung Cancer. *The oncologist*. 2016; 21: 119–26. [PubMed: 26621041]
16. Baider L, Andritsch E, Uziely B, et al. Effects of age on coping and psychological distress in women diagnosed with breast cancer: review of literature and analysis of two different geographical settings. *Critical reviews in oncology/hematology*. 2003; 46: 5–16. [PubMed: 12672514]
17. Derks W, Leeuw JR, Hordijk GJ and Winnubst JA. Differences in coping style and locus of control between older and younger patients with head and neck cancer. *Clinical otolaryngology : official journal of ENT-UK; official journal of Netherlands Society for Oto-Rhino-Laryngology & Cervico-Facial Surgery*. 2005; 30: 186–92.
18. Nipp RD, El-Jawahri A, Fishbein JN, et al. The relationship between coping strategies, quality of life, and mood in patients with incurable cancer. *Cancer*. 2016; 122: 2110–6. [PubMed: 27089045]
19. Goldzweig G, Andritsch E, Hubert A, et al. How relevant is marital status and gender variables in coping with colorectal cancer? A sample of middle-aged and older cancer survivors. *Psycho-oncology*. 2009; 18: 866–74. [PubMed: 19061195]
20. Temel JS, Greer JA, El-Jawahri A, et al. Effects of Early Integrated Palliative Care in Patients With Lung and GI Cancer: A Randomized Clinical Trial. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2017; 35: 834–41. [PubMed: 28029308]
21. Cella DF, Tulsky DS, Gray G, et al. The Functional Assessment of Cancer Therapy scale: development and validation of the general measure. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 1993; 11: 570–9. [PubMed: 8445433]
22. Kroenke K, Spitzer RL and Williams JB. The PHQ-9: validity of a brief depression severity measure. *Journal of general internal medicine*. 2001; 16: 606–13. [PubMed: 11556941]
23. Carver CS. You want to measure coping but your protocol's too long: consider the brief COPE. *International journal of behavioral medicine*. 1997; 4: 92–100. [PubMed: 16250744]
24. Carver CS, Scheier MF and Weintraub JK. Assessing coping strategies: a theoretically based approach. *Journal of personality and social psychology*. 1989; 56: 267–83. [PubMed: 2926629]
25. Hagan TL, Fishbein JN, Nipp RD, et al. Coping in Patients With Incurable Lung and Gastrointestinal Cancers: A Validation Study of the Brief COPE. *Journal of pain and symptom management*. 2017; 53: 131–8. [PubMed: 27725249]
26. Yancik R Cancer burden in the aged: an epidemiologic and demographic overview. *Cancer*. 1997; 80: 1273–83. [PubMed: 9317180]
27. Blank TO and Bellizzi KM. A gerontologic perspective on cancer and aging. *Cancer*. 2008; 112: 2569–76. [PubMed: 18428204]

28. Brighi N, Balducci L and Biasco G. Cancer in the elderly: is it time for palliative care in geriatric oncology? *Journal of geriatric oncology*. 2014; 5: 197–203. [PubMed: 24560041]
29. Hurria A, Gupta S, Zauderer M, et al. Developing a cancer-specific geriatric assessment: a feasibility study. *Cancer*. 2005; 104: 1998–2005. [PubMed: 16206252]
30. Marshall SW. Power for tests of interaction: effect of raising the Type I error rate. *Epidemiol Perspect Innov*. 2007; 4: 4. [PubMed: 17578572]
31. Wang R and Ware JH. Detecting moderator effects using subgroup analyses. *Prev Sci*. 2013; 14: 111–20. [PubMed: 21562742]
32. Nipp RD, Greer JA, El-Jawahri A, et al. Coping and Prognostic Awareness in Patients With Advanced Cancer. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2017; JCO2016713404.
33. Cheung WY, Le LW, Gagliese L and Zimmermann C. Age and gender differences in symptom intensity and symptom clusters among patients with metastatic cancer. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer*. 2011; 19: 417–23. [PubMed: 20333411]
34. Linden W, Vodermaier A, Mackenzie R and Greig D. Anxiety and depression after cancer diagnosis: prevalence rates by cancer type, gender, and age. *Journal of affective disorders*. 2012; 141: 343–51. [PubMed: 22727334]
35. Mor V, Allen S and Malin M. The psychosocial impact of cancer on older versus younger patients and their families. *Cancer*. 1994; 74: 2118–27. [PubMed: 8087779]
36. Yancik R Population aging and cancer: a cross-national concern. *Cancer journal*. 2005; 11: 437–41.
37. Cella D, Eton DT, Fairclough DL, et al. What is a clinically meaningful change on the Functional Assessment of Cancer Therapy-Lung (FACT-L) Questionnaire? Results from Eastern Cooperative Oncology Group (ECOG) Study 5592. *Journal of clinical epidemiology*. 2002; 55: 285–95. [PubMed: 11864800]
38. Cella D, Eton DT, Lai JS, Peterman AH and Merkel DE. Combining anchor and distribution-based methods to derive minimal clinically important differences on the Functional Assessment of Cancer Therapy (FACT) anemia and fatigue scales. *Journal of pain and symptom management*. 2002; 24: 547–61. [PubMed: 12551804]
39. Curry C, Cossich T, Matthews JP, Beresford J and McLachlan SA. Uptake of psychosocial referrals in an outpatient cancer setting: improving service accessibility via the referral process. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer*. 2002; 10: 549–55. [PubMed: 12324810]
40. Mystakidou K, Tsilika E, Parpa E, et al. Demographic and clinical predictors of spirituality in advanced cancer patients: a randomized control study. *Journal of clinical nursing*. 2008; 17: 1779–85. [PubMed: 18592623]
41. Jacobs-Lawson JM, Schumacher MM, Hughes T and Arnold S. Gender differences in psychosocial responses to lung cancer. *Gender medicine*. 2010; 7: 137–48. [PubMed: 20435276]

**What is already known about the topic?**

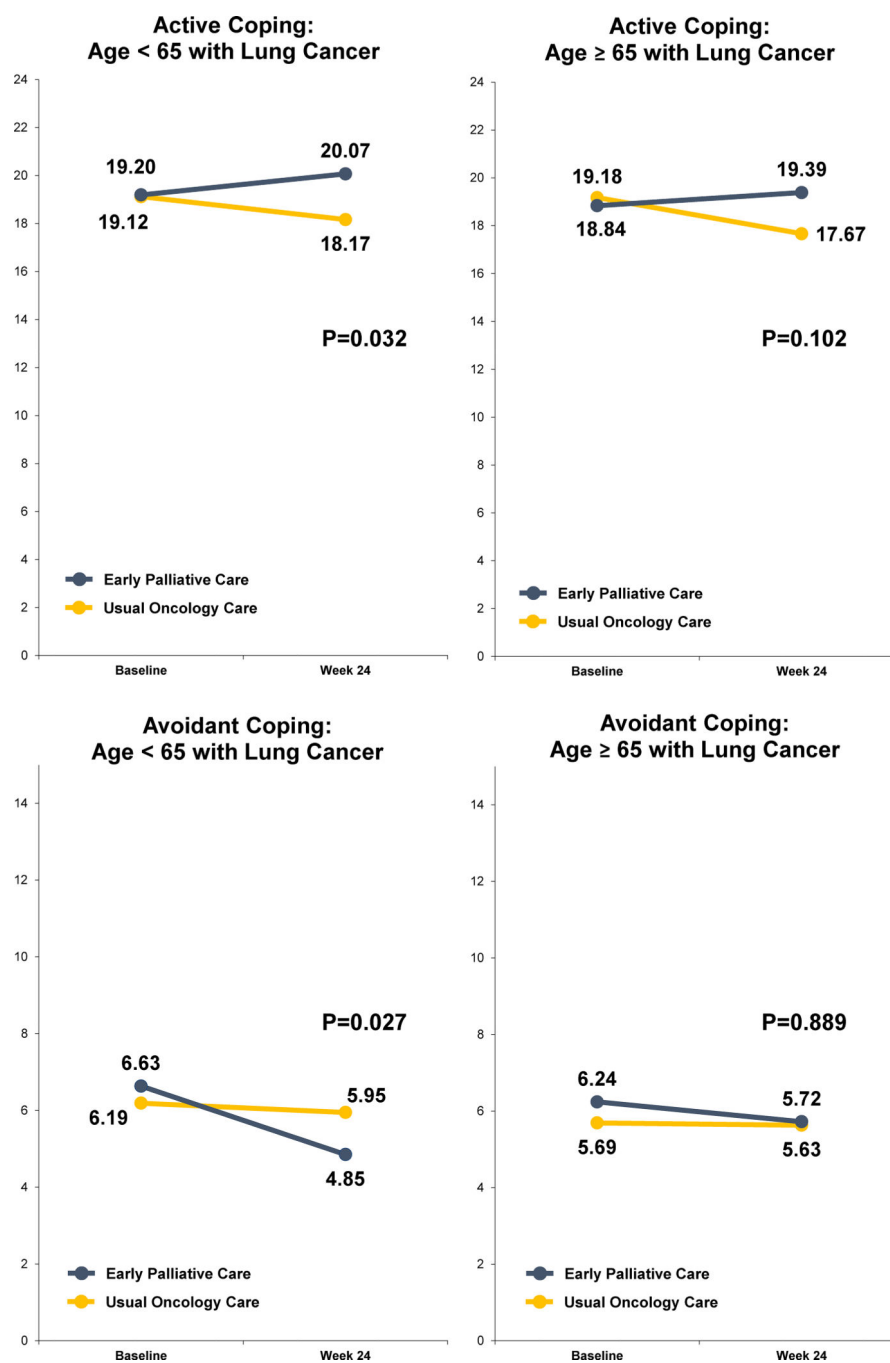
- Early integration of palliative care with routine oncology care often benefits patients with advanced cancer.
- Little data exist to clarify whether certain subgroups of patients are more or less likely to experience the benefits of early palliative care.

**What this paper adds**

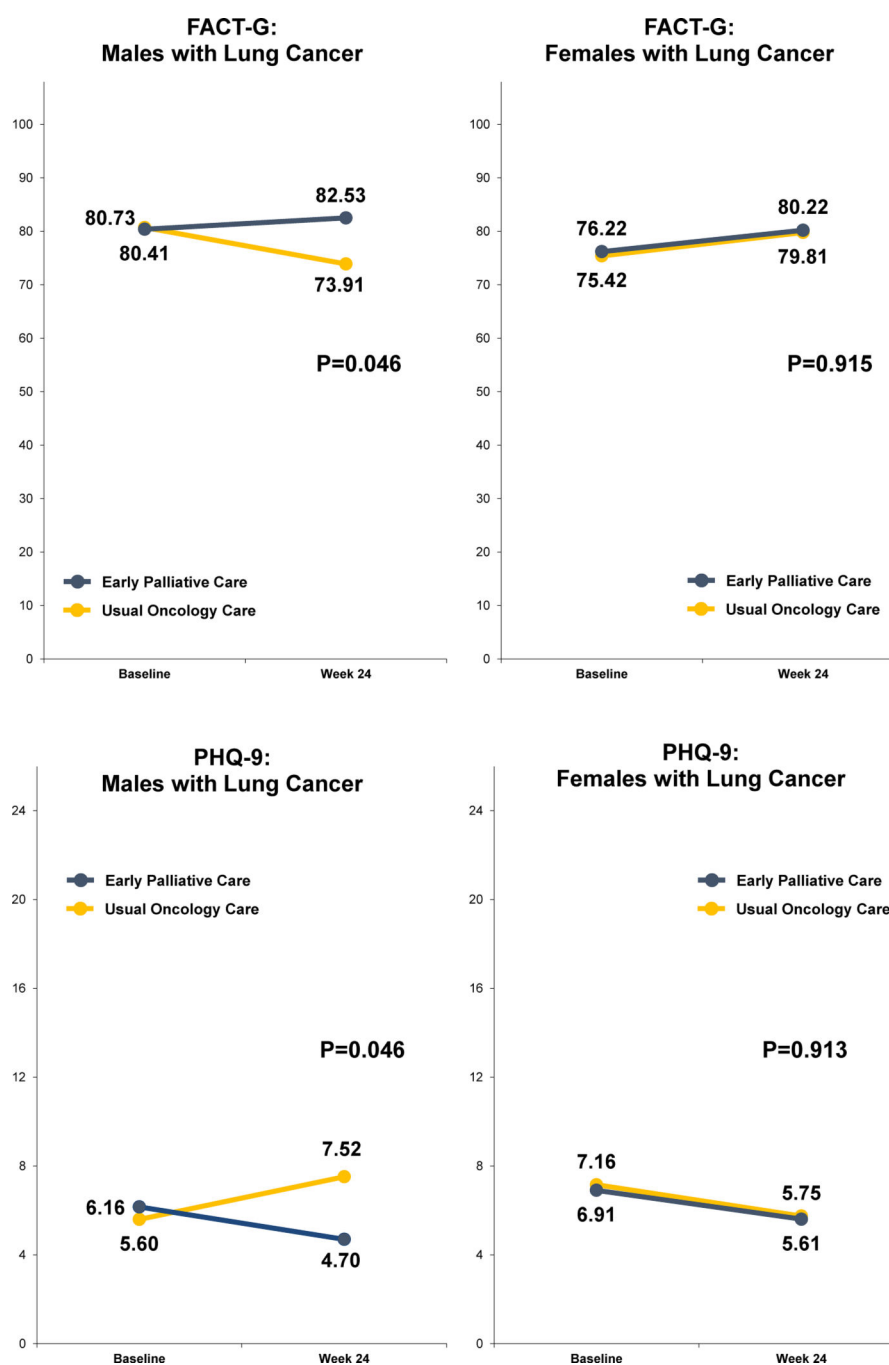
- Using data from a randomized trial of early palliative care, we demonstrated that age and sex moderate the effects of early palliative care on quality of life, depression symptoms, and coping strategies in patients with advanced lung cancer.
- Specifically, we found that younger patients with lung cancer who received early palliative care reported increased use of active coping and decreased use of avoidant coping, but the effects of early palliative care on these outcomes were not significant for older patients.
- Male patients with lung cancer who received early palliative care reported better quality of life and lower depression scores, but the effects of early palliative care on these outcomes were not significant for female patients.

**Implications for practice, theory or policy**

- These results suggest that patients' clinical and sociodemographic factors may modify both their cancer experience and palliative care needs.
- Our findings underscore the importance of accounting for age and sex in future efforts to develop supportive care interventions tailored to the unique needs of patients with advanced cancer.



**Figure 1.**  
Use of Active and Avoidant Coping Strategies from Baseline to Week 24 within Age Subgroups



**Figure 2.** QOL and Depression Symptom Scores from Baseline to Week 24 within Sex Subgroups  
Abbreviations: QOL, quality of life; FACT-G, Functional Assessment of Cancer Therapy-General; PHQ-9, Patient Health Questionnaire 9.

**Table 1.**

Baseline Characteristics of Study Participants, N=350

Clinical Characteristics	Entire Cohort (N=350)		Gastrointestinal Cancer (N=159)		Lung Cancer (N=191)		P
	N	%	N	%	N	%	
<b>Age, years – mean (SD)</b>	64.84 (10.88)		64.91 (11.16)		64.78 (10.68)		0.905
<b>Age 65</b>	181	51.7	86	54.1	95	49.7	0.453
<b>Sex</b>							
Male	189	54.0	99	62.3	90	47.1	0.005
Female	161	46.0	60	37.7	101	52.9	
<b>Race</b>							
White	323	92.3	145	91.2	178	93.2	0.615
African American	10	2.9	4	2.5	6	3.1	
Asian	8	2.3	4	2.5	4	2.1	
American Indian/Alaska Native	4	1.1	2	1.3	2	1.0	
Other	5	1.4	4	2.5	1	0.5	
<b>Hispanic/Latino ethnicity</b>	9	2.6	5	3.2	4	2.1	0.737
<b>Smoking History</b>							
<10 pack years	142	40.6	93	58.5	49	25.7	<0.001
10 pack years	188	53.7	50	31.4	138	72.3	
Unknown	20	5.7	16	10.1	4	2.1	
<b>ECOG performance status</b>							
0	88	25.1	46	28.9	42	22.0	0.320
1	231	66.0	99	62.3	132	69.1	
2	31	8.9	14	8.8	17	8.9	
<b>Initial cancer therapy</b>							
Chemotherapy	278	79.4	147	92.5	131	68.6	<0.001
Radiation *	67	19.1	8	5.0	59	30.9	
Chemoradiotherapy	3	0.9	3	1.9	0	0.0	
None	2	0.6	1	0.6	1	0.5	
<b>Religion</b>							
Catholic	201	57.4	84	53.2	117	61.3	0.083
Protestant	62	17.7	29	18.4	33	17.3	
Jewish	16	4.6	6	3.8	10	5.2	
Muslim	3	0.9	1	0.6	2	1.0	
None	41	11.7	19	12.0	22	11.5	
Other	26	7.4	19	12.0	7	3.7	
Missing	1	0.3					
<b>Relationship Status</b>							
Married	245	70.0	114	71.7	131	68.6	0.427
Divorced	36	10.3	12	7.5	24	12.6	
Widowed	35	10.0	18	11.3	17	8.9	
Single	34	9.7	15	9.4	19	9.9	



Clinical Characteristics	<u>Entire Cohort (N=350)</u>		<u>Gastrointestinal Cancer (N=159)</u>		<u>Lung Cancer (N=191)</u>		P
	N	%	N	%	N	%	
<b>Have dependent children</b>	44	12.6	20	12.6	24	12.6	1.000
<b>Education level</b>							
High school	131	37.4	50	31.4	81	42.4	0.036
> High school	219	62.6	109	68.6	110	57.6	
<b>Income Level</b>							
\$50,000	133	38.0	55	36.9	78	45.1	0.142
>\$50,000	189	54.0	94	63.1	95	54.9	
Missing	28	8.0					

Abbreviations: SD, standard deviation; ECOG, Eastern Cooperative Oncology Group.

\* one person who received transarterial chemoembolization (TACE) as their initial cancer therapy is included within the radiation category

**Table 2.**

Effects of Early Palliative Care on QOL, Depression Symptoms, and Coping Strategies from Baseline to Week 24 by Age within Cancer Type

<b>Lung Cancers</b>								
<b>Outcomes</b>	<b>Age &lt;65</b>				<b>Age 65</b>			
	<b>B (SE)</b>	<b>95% CI</b>	<b>Beta</b>	<b>P</b>	<b>B (SE)</b>	<b>95% CI</b>	<b>Beta</b>	<b>P</b>
<b>FACT-G</b>	5.85 (3.39)	−0.93 to 12.62	0.17	0.090	4.01 (3.66)	−3.32 to 11.34	0.13	0.277
<b>PHQ-9</b>	−1.50 (1.25)	−4.00 to 1.01	−0.13	0.237	−1.18 (1.09)	−3.36 to 1.00	−0.12	0.281
<b>Avoidant Coping</b>	−0.97 (0.41)	−1.78 to −0.16	−0.23	0.020	0.01 (0.42)	−0.83 to 0.84	0.00	0.987
<b>Active Coping</b>	1.74 (0.74)	0.26 to 3.23	0.26	0.022	1.98 (1.00)	−0.03 to 3.98	0.24	0.053
<b>Gastrointestinal Cancers</b>								
<b>Outcomes</b>	<b>Age &lt;65</b>				<b>Age 65</b>			
	<b>B (SE)</b>	<b>95% CI</b>	<b>Beta</b>	<b>P</b>	<b>B (SE)</b>	<b>95% CI</b>	<b>Beta</b>	<b>P</b>
<b>FACT-G</b>	4.72 (3.51)	−2.33 to 11.78	0.15	0.185	4.77 (3.39)	−2.04 to 11.58	0.17	0.166
<b>PHQ-9</b>	−0.29 (1.19)	−2.68 to 2.10	−0.03	0.809	−0.67 (1.26)	−3.20 to 1.87	−0.06	0.599
<b>Avoidant Coping</b>	−0.23 (0.50)	−1.22 to 0.77	−0.06	0.647	−0.73 (0.56)	−1.86 to 0.39	−0.17	0.197
<b>Active Coping</b>	−0.45 (0.85)	−2.17 to 1.27	−0.06	0.601	0.94 (0.90)	−0.87 to 2.74	0.15	0.303

Abbreviations: QOL, quality of life; SE, standard error; 95% CI, 95% confidence interval; FACT-G, Functional Assessment of Cancer Therapy-General; PHQ-9, Patient Health Questionnaire 9.

**Table 3.**

Effects of Early Palliative Care on QOL, Depression Symptoms, and Coping Strategies from Baseline to Week 24 by Sex within Cancer Type

<b>Lung Cancers</b>								
<b>Outcomes</b>	<b>Male</b>				<b>Female</b>			
	<b>B (SE)</b>	<b>95% CI</b>	<b>Beta</b>	<b>P</b>	<b>B (SE)</b>	<b>95% CI</b>	<b>Beta</b>	<b>P</b>
<b>FACT-G</b>	9.31 (3.66)	1.98 to 16.65	0.27	0.014	0.60 (3.29)	−5.95 to 7.16	0.02	0.854
<b>PHQ-9</b>	−2.82 (1.13)	−5.08 to −0.55	−0.26	0.016	0.03 (1.16)	−2.28 to 2.34	0.00	0.979
<b>Avoidant Coping</b>	−0.43 (0.36)	−1.15 to 0.30	−0.09	0.243	−0.35 (0.40)	−1.16 to 0.45	−0.10	0.383
<b>Active Coping</b>	1.61 (0.75)	0.10 to 3.13	0.26	0.038	2.14 (0.90)	0.34 to 3.95	0.26	0.021
<b>Gastrointestinal Cancers</b>								
<b>Outcomes</b>	<b>Male</b>				<b>Female</b>			
	<b>B (SE)</b>	<b>95% CI</b>	<b>Beta</b>	<b>P</b>	<b>B (SE)</b>	<b>95% CI</b>	<b>Beta</b>	<b>P</b>
<b>FACT-G</b>	3.10 (2.98)	−2.85 to 9.04	0.11	0.302	7.22 (4.18)	−1.25 to 15.69	0.21	0.092
<b>PHQ-9</b>	0.10 (1.04)	−1.96 to 2.17	0.01	0.921	−1.14 (1.62)	−4.43 to 2.15	−0.10	0.487
<b>Avoidant Coping</b>	−0.33 (0.41)	−1.15 to 0.49	−0.08	0.430	−0.67 (0.74)	−2.17 to 0.83	−0.14	0.373
<b>Active Coping</b>	0.84 (0.78)	−0.72 to 2.41	0.12	0.286	−1.28 (1.17)	−3.65 to 1.10	−0.16	0.283

Abbreviations: QOL, quality of life; SE, standard error; 95% CI, 95% confidence interval; FACT-G, Functional Assessment of Cancer Therapy-General; PHQ-9, Patient Health Questionnaire 9.