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ORIGINAL REPORT

Effects of Early Integrated Palliative Care in Patients With Lung and GI Cancer: A Randomized Clinical Trial

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ABSTRACT

Purpose

We evaluated the impact of early integrated palliative care (PC) in patients with newly diagnosed lung and GI cancer.

Patients and Methods

We randomly assigned patients with newly diagnosed incurable lung or noncolorectal GI cancer to receive either early integrated PC and oncology care (n = 175) or usual care (n = 175) between May 2011 and July 2015. Patients who were assigned to the intervention met with a PC clinician at least once per month until death, whereas those who received usual care consulted a PC clinician upon request. The primary end point was change in quality of life (QOL) from baseline to week 12, per scoring by the Functional Assessment of Cancer Therapy-General scale. Secondary end points included change in QOL from baseline to week 24, change in depression per the Patient Health Questionnaire-9, and differences in end-of-life communication.

Results

Intervention patients (v usual care) reported greater improvement in QOL from baseline to week 24 (1.59 v −3.40; P = .010) but not week 12 (0.39 v −1.13; P = .339). Intervention patients also reported lower depression at week 24, controlling for baseline scores (adjusted mean difference, −1.17; 95% CI, −2.33 to −0.01; P = .048). Intervention effects varied by cancer type, such that intervention patients with lung cancer reported improvements in QOL and depression at 12 and 24 weeks, whereas usual care patients with lung cancer reported deterioration. Patients with GI cancers in both study groups reported improvements in QOL and mood by week 12. Intervention patients versus usual care patients were more likely to discuss their wishes with their oncologist if they were dying (30.2% v 14.5%; P = .004).

Conclusion

For patients with newly diagnosed incurable cancers, early integrated PC improved QOL and other salient outcomes, with differential effects by cancer type. Early integrated PC may be most effective if targeted to the specific needs of each patient population.

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INTRODUCTION

Growing evidence supports a new role for palliative care (PC)–trained specialists in the outpatient care of patients with advanced cancer.[1] The aim of this research has been to improve symptom burden and quality of life (QOL) in these patients with high morbidity and incurable disease.[2] Several randomized trials have shown that simultaneous delivery of palliative and oncology care in the outpatient setting improves patient-reported outcomes.[3] For example, in patients with advanced cancer and a limited life expectancy, both telephone-based and in-person PC interventions led to improved QOL, reduced symptom burden, and greater satisfaction with care[4-6]; however, the impact of providing PC early in the course of disease for patients with newly diagnosed advanced cancers has received less attention. In one trial of patients with newly diagnosed metastatic non–small-cell lung cancer (NSCLC), early integrated PC significantly improved QOL, depression symptoms, and illness understanding.[7,8] Additional studies are needed to confirm these findings in diverse cancer populations with distinct disease trajectories.

Whereas improving patient QOL and symptom burden are key goals of any supportive care intervention, the practice of PC encompasses more

than just symptom management.[9] Patients with advanced cancer often fail to understand the intent of their cancer treatment and rarely engage in discussions about their preferences for care at the end of life (EOL).[10,11] Such misperceptions are associated with worse EOL-care outcomes.[10-12] PC clinicians are trained to help patients understand their prognosis and treatment goals and to facilitate informed decisions about their care throughout the illness trajectory and at EOL.[13] Through early integration, PC clinicians are positioned to support patients and oncologists in communicating about prognosis, treatment goals, and care preferences over time.

The goal of this study was to evaluate the effect of early integrated PC on patient-reported outcomes in a large cohort of patients with newly diagnosed, incurable cancers. We hypothesized that patients who were randomly assigned to the intervention would report better QOL, lower rates of depression, improved prognostic understanding, and more frequent discussions about their EOL-care preferences compared with those who were assigned to usual care.

PATIENTS AND METHODS

Study Design

We enrolled patients with newly diagnosed incurable cancers from Massachusetts General Hospital (MGH) in a nonblinded, randomized trial of early PC integrated with oncology care compared with usual oncology care. The Dana-Farber Cancer Institute/Harvard Cancer Center Institutional Review Board approved the study protocol, and all patients provided written informed consent.

Patients

Patients were eligible to participate if they were within 8 weeks of a diagnosis of incurable lung (NSCLC, small-cell, or mesothelioma) or noncolorectal GI (pancreatic, esophageal, gastric, or hepatobiliary) cancer. Patients were also required to receive their care at MGH, be ≥ 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. We excluded patients who were already receiving PC services, needed immediate referral for PC or hospice, or who had significant psychiatric or other comorbid disease prohibiting participation.

Study staff screened consecutive patients who presented to the oncology clinics and notified clinicians via e-mail when patients were eligible to participate. At the time of visit, study staff placed a reminder about eligibility on patient charts. Oncology clinicians invited their patients to enroll in the study.

Random Assignment

The Office of Data Quality randomly assigned patients in a 1:1 fashion to receive early integrated PC and oncology care versus usual oncology care, stratified by cancer type, using a computer-generated number sequence, which was concealed until after group assignment.

Procedures

Patients who were assigned to early PC met with a member of the outpatient PC team within 4 weeks of enrollment and at least once per month until death. Consisting of physicians and advanced practice nurses, the MGH outpatient team practices per guidelines of the National Consensus Project for Quality Palliative Care.[14] PC clinicians contacted patients via telephone when an in-person visit was not possible. The patient, oncologist, or PC clinician could schedule additional PC visits at their discretion. Finally, for patients who were admitted to MGH, the inpatient PC team observed them throughout their hospitalization.

Patients who were assigned to usual oncology care were able to meet with a PC clinician only upon request by the oncologist, patient, or family. When these patients received PC services, they did not cross study groups or follow the intervention protocol. All patients, regardless of group assignment, continued to receive routine oncology care throughout the study period.

Patient-Reported Outcome Measures

We measured QOL with the 27-item Functional Assessment of Cancer Therapy-General (FACT-G) scale, which assesses four dimensions of QOL (physical, functional, emotional, and social well-being).[15] To evaluate mood and anxiety, patients completed the Patient Health Questionnaire-9 (PHQ-9) and the Hospital Anxiety and Depression Scale (HADS).[16,17] The PHQ-9 is a nine-item measure that detects symptoms of major depressive disorder according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders-IV, with higher scores indicating worse depression.[17] The 14-item HADS consists of two subscales that assess anxiety and depression symptoms. Subscale scores range from 0 (no distress) to 21 (maximum distress).

We used the Prognosis and Treatment Perceptions Questionnaire developed by El-Jawahri et al[18] to measure patients' understanding of their prognosis and report of their communication with oncologists. The 13 items inquire about patient information preferences, perceptions of their prognosis and health status, and communication about their prognosis and EOL preferences.

Data Collection

Patients completed a demographic questionnaire and baseline self-report measures after providing written informed consent and before random assignment. Follow-up assessments occurred at 12 weeks and 24 weeks(or within 3 weeks of those time points). Protocol staff who were separate from the research team administered study questionnaires. Patients who were unable to complete questionnaires in clinic received the questionnaires by e-mail or mail. In addition, PC clinicians used a study-specific, Web-based data capture tool to access a standardized template and record the focus of their clinic visits after each outpatient encounter and once during any hospitalization.

Statistical Analysis

We performed statistical analyses using STATA software (version 9.3; STATA, College Station, TX; Computing Resource Center, Santa Monica, CA) and R software (version 3.3.1; The R Foundation, Vienna, Austria). Data obtained through May 2016 were included. The primary outcome was change in FACT-G score from baseline to 12 weeks; a 4- to 5-point change in FACT-G score is considered clinically meaningful. We estimated that with 280 patients, the study would have 80% power to detect a 4-point difference in the change in FACT-G scores from baseline to 12 weeks between study groups (with $P < .05$). Given the rate of missing data observed in our previous study, we increased our sample size to 350 patients.

To examine QOL and mood we used independent-samples t tests and analysis of covariance (ANCOVA) models that controlled for baseline criterion scores and potential confounders such as age and comorbidity, which were imbalanced between groups and associated with outcomes of interest. We also used ANCOVA to explore whether the effect of intervention on outcomes varied by cancer cohort, that is, cancer cohort × group assignment interaction. Observing an interaction effect ($P < .15$),[19] we then conducted separate subgroup analyses in the lung and GI cancer cohorts with ANCOVA to assess the effect of intervention on QOL and mood.

We also compared patient-reported outcomes between the two groups by using a terminal decline joint modeling approach, which models the trend in outcomes backward from death, rather than prospectively from enrollment[20]. We did not prespecify the use of this approach in our protocol as it was first published in 2013, after initiation of this study; however, this technique offers an advantageous approach to account for deterioration in patient-reported outcomes closer to death and uses a mixed-effects model for longitudinal outcomes to provide valid estimates

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for missing data.[20] We estimated terminal decline and survival distributions with semiparametric models, comparing QOL and mood between study groups at 2, 4, and 6 months before death. All models adjusted for baseline criterion scores and potential confounders such as age and comorbidity. Given the observed interaction effect between cancer type and intervention effect, we also conducted subgroup analyses in the lung and GI cancer cohorts using terminal decline.

RESULTS

Baseline Characteristics

Three hundred fifty patients enrolled in the study (Appendix Fig A1, online only) between May 2, 2011 and July 20, 2015. Patients were mostly white (92.3%), with a mean age of 64.84 years (standard deviation, 10.88 years), and 54.0% were male. Intervention patients were slightly older and had greater comorbidities than did those in the usual care group (Table 1).

PC Visits

The mean number of PC visits by 24 weeks was 6.54 (range, 0 to 14) in the intervention group and 0.89 visits (range, 0 to 7) in the usual care group. The PC team met with 20.0% and 34.3% of usual care patients by weeks 12 and 24, respectively. Figure 1 depicts the number of PC visits by study group and the content PC clinicians addressed with intervention patients by 24 weeks.

QOL and Mood

Intervention patients reported a mean 0.39-point increase in FACT-G scores from baseline to 12 weeks compared with usual care patients who reported a 1.13-point decrease from baseline (t[296] = −0.96; SE = 1.59; P = .339; Cohen's d, 0.11). At 24 weeks, intervention patients reported a 1.59-point increase in FACT-G scores from baseline whereas usual care patients reported a 3.40-point decrease from baseline (t[238] = −2.59; SE = 1.93; P = .010; Cohen's d, 0.33). Patient PHQ-9, HADS-Depression, and HADS-Anxiety scores did not differ significantly between study groups from baseline to weeks 12 or 24; however, ANCOVA models that controlled for baseline variables demonstrated significant differences that favored the intervention for FACT-G and PHQ-9 scores at 24 weeks (Table 2). Using the terminal decline model, intervention participants had significantly higher QOL (FACT-G) and lower depression symptom (PHQ-9) scores at 2 and 4 months, but not at 6 months, before death (Table 3). Use of psychosocial services, including psychiatry, psychology, and social work, did not differ between study groups (data not shown).

Prognostic Understanding and Communication

At 12 weeks, similar proportions of patients in both study groups reported that their primary goal of cancer treatment was cure (intervention, 28.7% [n = 41 of 143] v usual care, 34.5% [n = 50 of 145]; P = .289). However, intervention patients were more likely than usual care patients to report that knowing about their prognosis was "very helpful" or "extremely helpful" in making decisions about treatment (96.5% [n = 110 of 114] v 89.8% [n = 115 of 128]; P = .043) and coping with the disease (97.3% [n = 108 of 111] v 83.6% [n = 107 of 128]; P < .001) at 12 weeks. At 24 weeks, more

intervention patients reported that they had discussed their EOL wishes with their oncologist compared with usual care patients (30.2% [n = 35 of 116] v 14.5% [n = 17 of 117]; P = .004). Study groups did not differ with respect to information preferences,

Table 1. Baseline Demographic and Clinical Characteristics

Characteristic	Usual Care (n = 175) No. (%)	Early PC (n = 175) No. (%)
Mean age, years (SD)	64.03 (10.46)	65.64 (11.26)
Male	98 (56.0)	91 (52.0)
Ethnicity		
White	167 (95.4)	156 (89.1)
American Indian	0 (0.0)	4 (2.3)
Asian	3 (1.7)	5 (2.9)
Black	4 (2.3)	6 (3.4)
Hispanic or Latino	2 (1.1)	7 (4.0)
Other	1 (0.6)	4 (2.3)
Religion		
Catholic	103 (59.2)	98 (56.0)
Protestant	36 (20.7)	26 (14.9)
Jewish	2 (1.1)	14 (8.0)
Muslim	2 (1.1)	1 (0.6)
None	21 (12.1)	20 (11.4)
Other	10 (5.7)	16 (9.1)
Relationship status		
Married or partnership	124 (70.9)	121 (69.1)
Single	17 (9.7)	17 (9.7)
Divorced or separated	18 (10.3)	18 (10.3)
Widowed	16 (9.1)	19 (10.9)
Education		
High school or less	73 (41.7)	58 (33.1)
Some or completed college	69 (39.4)	76 (43.4)
Graduate school	33 (18.9)	41 (23.4)
Cancer type		
Lung	96 (54.9)	95 (54.3)
Non–small-cell	74	80
Small-cell	17	13
Neuroendocrine	3	1
Mesothelioma	2	1
EGFR mutation	10	19
ALK translocation	4	4
GI	79 (45.1)	80 (45.7)
Pancreatic	43	44
Esophageal/GE junction	17	15
Gastric	4	3
Hepatobiliary	15	18
Smoking status		
Never smoker or < 10 pack-years	67 (38.3)	75 (42.9)
Current or former smoker	95 (54.3)	93 (53.1)
Unknown	13 (7.4)	7 (4.0)
ECOG PS		
0	43 (24.6)	45 (25.7)
1	115 (65.7)	116 (66.3)
2	17 (9.7)	14 (8.0)
Charlson Comorbidity Index score, mean (SD)	6.73 (1.39)	7.03 (1.35)
FACT-G score, mean (SD)	77.79 (15.46)	78.84 (14.90)
PHQ-9 score, mean (SD)	6.50 (5.19)	6.39 (5.49)
HADS-Depression subscale score, mean (SD)	4.58 (3.73)	4.72 (4.28)
HADS-Anxiety subscale score, mean (SD)	5.57 (3.88)	5.05 (3.95)

Abbreviations: ALK, anaplastic lymphoma kinase; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; FACT-G, Functional Assessment of Cancer Therapy-General scale; GE, gastroesophageal; HADS, Hospital Anxiety and Depression Scale; PC, palliative care; PHQ-9, Patient Health Questionnaire-9; SD, standard deviation.
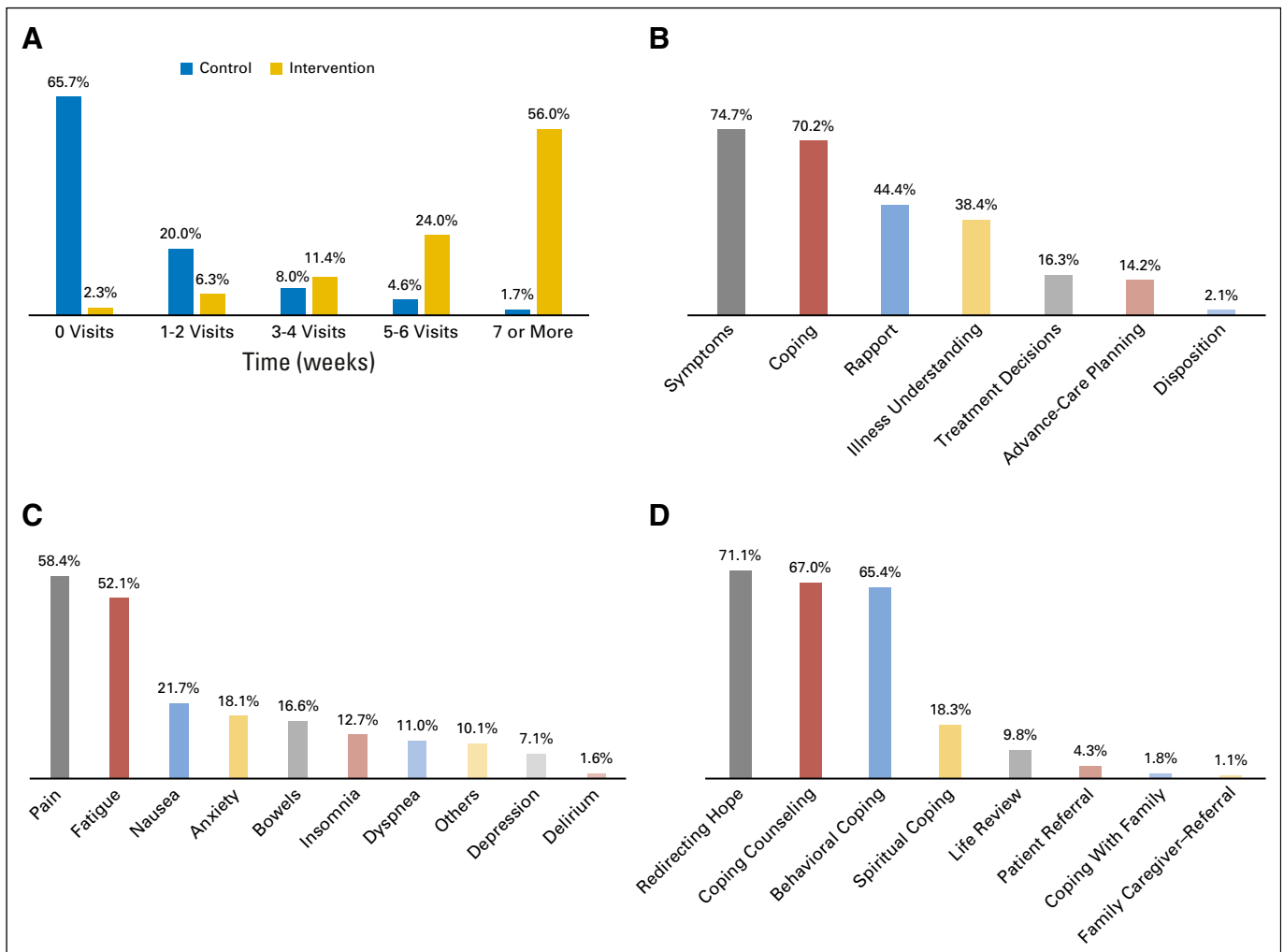
Fig 1. Frequency and content of palliative care (PC) visits. (A) Number of PC visits by study group. Bars represent the percentage of PC visits for all study patients within 24 weeks. Four intervention patients withdrew from the study before their first scheduled PC visit. (B) Content areas of PC visits with intervention patients per PC clinician documentation. PC clinicians used a standardized template to electronically document the focus of their intervention visits after each encounter. Bars represent the proportion of PC visits that focused on each content area within 24 weeks. (C) Bars represent the proportion of visits that each symptom was addressed when PC noted symptoms as a visit focus. (D) Bars represent the proportion of visits that each topic was addressed when PC noted coping as a visit focus.

frequency of conversations about prognosis, or rating of the quality of information.

Effect of PC Intervention by Cancer Type

Figure 2 depicts QOL and depression data longitudinally by cancer cohort. Effects of the intervention varied by cancer cohort over time for both FACT-G (cancer cohort × group assignment interaction F[1,291] = 2.94; P = .088) and PHQ-9 (cancer cohort × group assignment interaction F[1,293] = 3.05; P = .082) scores. We therefore conducted separate subgroup analyses to examine differences in outcomes for the lung and GI cancer cohorts. ANCOVA models that controlled for baseline variables demonstrated significant intervention effects in the lung cancer cohort for FACT-G and PHQ-9 scores at both 12 and 24 weeks, but not in the GI cohort (Table 2).

By using the terminal decline model, intervention participants with lung cancer had significantly higher QOL and lower depression symptom scores at 2, 4, and 6 months before

death. In contrast, QOL and depression did not differ between study groups in the GI cancer cohort before death (Table 3). Given these results, we explored characteristics between patients with lung and GI cancer and found no differences in baseline measures or in the number of PC visits among those patients who received intervention (Appendix Table A1, online only). However, the GI cancer cohort had a higher proportion of male patients and a greater number of hospitalizations from baseline to week 24 compared with the lung cancer cohort.

DISCUSSION

The results from this trial add to the growing literature on the benefits of integrating PC services earlier in the course of disease for patients with advanced cancer. We not only confirmed previous findings that early integrated PC improves QOL and mood in patients with incurable cancers, but also that these positive effects on

Table 2. Intervention Effects on 12- and 24-Week QOL and Mood

Cohort	No.	Usual Care, Adjusted Mean (95% CI)	Early Care, Adjusted Mean (95% CI)	Adjusted Mean Difference (SE)	95% CI	P
Entire sample						
12-week outcomes						
FACT-G score	298	77.70 (75.77 to 79.63)	80.10 (78.11 to 82.08)	2.40 (1.41)	(−0.38 to 5.18)	.091
PHQ-9 score	300	6.33 (5.65 to 7.01)	5.55 (4.85 to 6.25)	−0.78 (0.50)	(−1.76 to 0.21)	.121
24-week outcomes						
FACT-G score	240	75.90 (73.59 to 78.21)	81.26 (78.89 to 83.63)	5.36 (1.69)	(2.04 to 8.69)	.002
PHQ-9 score	239	6.72 (5.91 to 7.53)	5.55 (4.72 to 6.37)	−1.17 (0.59)	(−2.33 to −0.01)	.048
Lung cancer						
12-week outcomes						
FACT-G score	159	74.37 (71.38 to 77.36)	79.41 (76.32 to 82.51)	5.04 (2.21)	(0.68 to 9.41)	.024
PHQ-9 score	161	7.21 (6.18 to 8.24)	5.61 (4.55 to 6.66)	−1.61 (0.76)	(−3.10 to −0.11)	.035
24-week outcomes						
FACT-G score	130	75.62 (72.18 to 79.07)	82.15 (78.81 to 85.48)	6.52 (2.48)	(1.62 to 11.42)	.010
PHQ-9 score	130	6.71 (5.90 to 7.53)	5.54 (4.72 to 6.37)	−1.17 (0.59)	(−2.33 to −0.01)	.048
GI cancer						
12-week outcomes						
FACT-G score	139	81.32 (79.01 to 83.63)	81.09 (78.74 to 83.45)	−0.23 (1.67)	(−3.53 to 3.08)	.892
PHQ-9 score	139	5.34 (4.45 to 6.23)	5.44 (4.53 to 6.35)	0.11 (0.64)	(−1.17 to 1.38)	.870
24-week outcomes						
FACT-G score	110	75.96 (72.76 to 79.15)	80.35 (76.85 to 83.85)	4.39 (2.39)	(−0.36 to 9.14)	.070
PHQ-9 score	109	6.57 (5.41 to 7.74)	6.19 (4.92 to 7.46)	−0.38 (0.87)	(−2.11 to 1.34)	.659

NOTE. Results of analysis of covariance models controlling for baseline values for the criterion outcome as well as potential confounders that are imbalanced between groups, that is, patient age and Charlson Comorbidity Index.

Abbreviations: FACT-G, Functional Assessment of Cancer Therapy-General scale; PC, palliative care; PHQ-9, Patient Health Questionnaire-9; QOL, quality of life.

patient outcomes vary by cancer type. We further identified new benefits of the integrated PC model in improving patients' ability to cope with their prognosis and in enhancing their communication about EOL-care preferences with clinicians. Of importance, these data elucidate key elements of the early PC intervention, encompassing much more than symptom management.

Given our prior study in patients with advanced NSCLC,[21] the primary outcome of this trial was change in QOL from baseline to 12 weeks; however, we did not detect a significant improvement in QOL with early integrated PC until the 24-week time point. These results are consistent with the three prior randomized trials of early PC that all failed to show a significant improvement in QOL at

Table 3. Intervention Effect on Quality of Life and Mood Measured Backward From Death*

Cohort	2 Months Before Death		4 Months Before Death		6 Months Before Death	
	Mean (95% CI)	P	Mean (95% CI)	P	Mean (95% CI)	P
Entire sample						
FACT-G score		.016		.011		.430
Early PC	75.67 (73.14 to 78.20)		82.06 (79.96 to 84.17)		81.44 (78.96 to 83.91)	
Usual care	71.44 (69.14 to 73.76)		78.22 (76.14 to 80.30)		79.99 (77.35 to 82.62)	
PHQ-9 score		.046		.042		.991
Early PC	7.04 (6.15 to 7.93)		6.17 (5.43 to 6.84)		5.36 (4.51 to 6.21)	
Usual care	8.29 (7.45 to 9.13)		6.86 (6.69 to 7.75)		5.37 (4.28 to 6.45)	
Lung cancer						
FACT-G score		.022		.010		.013
Early PC	75.74 (72.21 to 79.27)		82.22 (78.99 to 85.44)		82.53 (79.52 to 85.53)	
Usual care	70.03 (66.65 to 73.41)		76.24 (73.04 to 79.45)		77.12 (74.14 to 80.45)	
PHQ-9 score		.009		.004		.011
Early PC	6.12 (4.91 to 7.32)		5.69 (4.73 to 6.65)		5.27 (4.30 to 6.23)	
Usual care	8.35 (7.18 to 9.52)		7.70 (6.76 to 8.64)		7.05 (6.10 to 8.00)	
GI cancer						
FACT-G score		.231		.258		.998
Early PC	76.23 (72.73 to 79.74)		81.97 (79.23 to 84.72)		81.87 (79.30 to 84.44)	
Usual care	73.52 (70.77 to 76.26)		79.79 (77.18 to 82.41)		81.88 (79.34 to 84.42)	
PHQ-9 score		.631		.594		.842
Early PC	7.85 (6.53 to 9.17)		5.94 (4.90 to 6.98)		5.28 (4.30 to 6.27)	
Usual care	7.44 (6.38 to 8.49)		5.55 (4.56 to 6.54)		5.14 (4.18 to 6.11)	

Abbreviations: FACT-G, Functional Assessment of Cancer Therapy-General scale; PC, palliative care; PHQ-9, Patient Health Questionnaire-9.

*Results of terminal decline models controlling for baseline values for the criterion outcome as well as potential confounders in baseline characteristics, that is, patient age and Charlson Comorbidity Index.
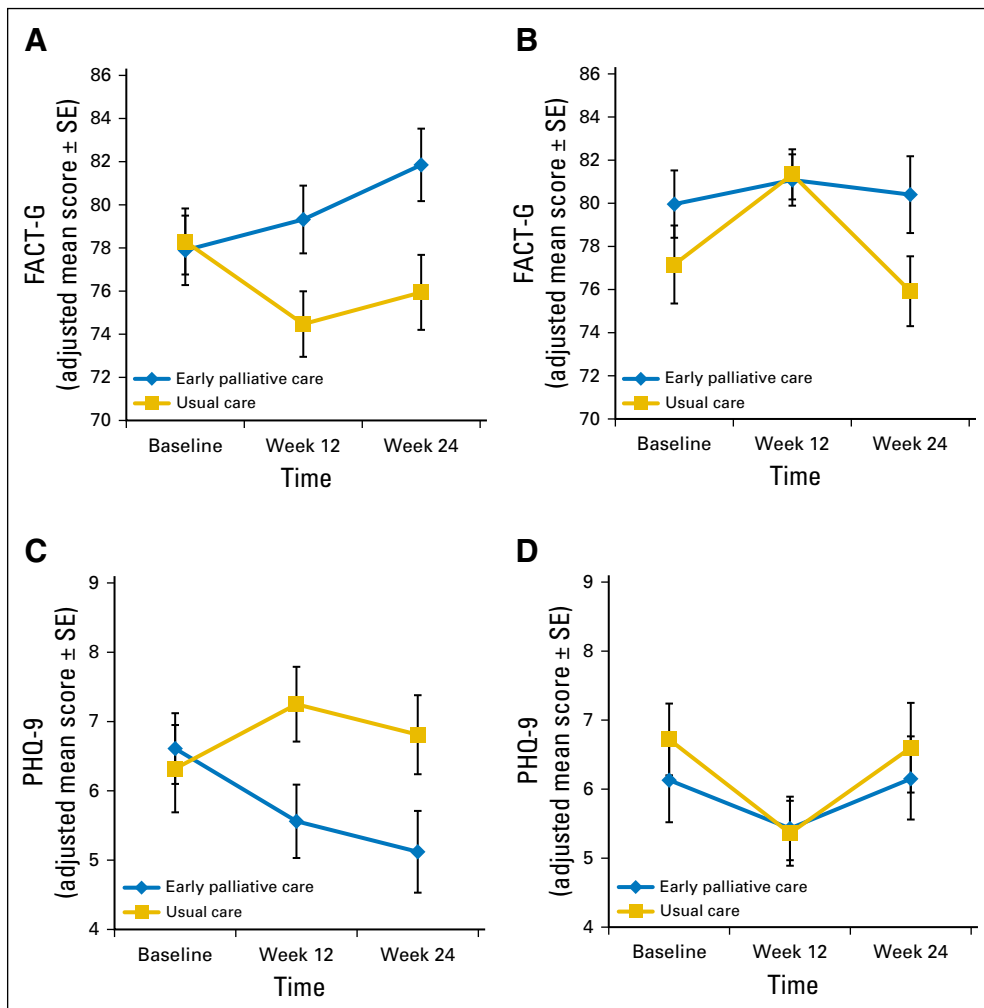
Fig 2. Trajectories of quality of life (QOL) and depression symptoms over time by cancer cohort. (A) QOL in lung cancer. (B) QOL in GI cancer. (C) Depression symptoms in lung cancer. (D) Depression symptoms in GI cancer. FACT-G, Functional Assessment of Cancer Therapy-General scale; PHQ-9, Patient Health Questionnaire-9.

12 weeks.[4,5,22] Similar to the Educate, Nurture, Advise, Before Life Ends (ENABLE) Project, our terminal decline analysis confirmed that patients assigned to early integrated PC reported better QOL and mood in the months before death.[4] Thus, longer follow-up might be needed to fully assess the effect of the early PC model on patient-reported outcomes.

Prior randomized trials of PC interventions included patients with different cancer diagnoses with considerable heterogeneity in their time from diagnosis, clinical course, and overall survival. Given these trials in mixed cancer populations, we did not expect differential outcomes by cancer type. Whereas subgroup analyses are exploratory, we did demonstrate differences in study outcomes between patients with lung and GI cancers. Similar to our previous study, patients with lung cancer who received usual care reported worsened QOL from baseline to 12 weeks, whereas intervention patients had improved QOL over this timeframe.[7] This QOL difference in the lung cancer cohort became even more pronounced by 24 weeks and in the months before death. In contrast, regardless of group assignment, the GI cohort reported an improvement in their QOL over the initial 12 weeks of the trial, with no differences in study outcomes in the months before death. Thus, the QOL and mood trajectories, as well as the impact of PC integration on these patient-reported outcomes, vary between patients with lung and GI cancers. Although further research is needed to understand these

differences, a possible explanation for these findings is that patients with GI cancer spent significantly more time in the hospital than did patients with lung cancer, which may have affected their QOL and mood. In future work, investigators should explore the role of targeted PC interventions to address the specialized needs of specific cancer populations with particular attention to appropriate timing for PC integration within the context of patients' illness trajectories.

This trial is the first, to our knowledge, to show an effect of early PC on patients' communication about EOL-care preferences. We observed that intervention patients were twice as likely to report that they had discussed their EOL-care wishes compared with usual care patients. Intervention patients were also more likely to report that knowing about their prognoses helped them make decisions about treatment and to cope with their illness. As a clinical care model, PC intervention in this trial was not strictly manualized.[5,7] In contrast, a recent study of a structured communication intervention delivered by PC clinicians in the intensive care unit failed to improve family caregiver–reported outcomes.[23] Allowing PC clinicians the freedom to address the concerns that are most salient for the patient may be the optimal approach to provide personalized care; however, this patient-centered approach has also made it challenging to describe the elements of early PC intervention. Results from this trial regarding both the nature of the

PC visits and the impact of early PC on patients' coping and communication shed new light on the key processes of this care model. Whereas symptom management is a core component of PC, providing patients with the skills they need to cope with and communicate about their life-threatening illness is another essential element of PC for patients with advanced cancer.

Our study has several limitations. First, patients and clinicians were not blinded to group assignment. Second, we did not anticipate the difference in QOL and mood trajectories between patients with lung and GI cancers; thus, we did not plan the sample size to evaluate outcomes by cancer subtype. Third, because usual care at our institution often entails involvement of PC in the outpatient setting, more than one third of patients who were assigned to usual care met with the PC team during the first 24 weeks of the study. This contact may have diluted the effect of the intervention, though such practice likely represents current national standards. Similarly, our PC team has been well integrated in our cancer center for the last decade, which has perhaps enhanced the PC skills of oncologists.[24] Lastly, we conducted the trial at a single institution with a predominantly white and English-speaking population, which may limit the generalizability of the results to other care settings and clinical populations.

Early integration of palliative and oncology care in patients with newly diagnosed incurable cancers improves QOL, reduces depression symptoms, and enhances coping with prognosis and communication about EOL-care preferences. These findings provide further evidence to support early integrated PC as the standard of care for patients with newly diagnosed incurable cancers. With the recent *Dying in America*[25] report strongly urging research to improve patient-clinician communication about EOL care, the finding that intervention patients were twice as likely as usual care patients to discuss EOL-care preferences is notable and timely. Although the outcomes of this trial demonstrate meaningful benefits of early PC, they raise new questions about how best to integrate and evaluate PC in populations with different disease and QOL trajectories. This study also highlights the complexities of studying supportive care interventions during a time of rapid advances in cancer treatment, as recent discoveries are having an undeniable impact on patient survival, but also perhaps on QOL and mood. Thus, further research is needed to define optimal PC delivery models that target the specific needs of different patient populations in the modern era of cancer therapeutics.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Effects of Early Integrated Palliative Care in Patients with Lung and GI Cancer: A Randomized Clinical Trial

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Appendix

Patients with incurable thoracic
and noncolorectal cancers (N = 2,753)

Did not meet inclusion criteria   (n = 2,261)
   Did not receive oncology care at institution (n = 1,715)
   Clinician reported patient needed
     palliative care or hospice   (n = 397)
   Did not speak English   (n = 51)
   ECOG PS > 2   (n = 44)
   Clinician reported study not appropriate   (n = 32)
   Died before next appointment   (n = 22)
  Study closed during eligibility period   (n = 12)

Eligible
patients (n = 480)

Not enrolled   (n = 130)
  Study not offered   (n = 13)
  Patient refused participation   (n = 117)

Patients enrolled
and randomly assigned (n = 350)

Allocated to early palliative care (n = 175)

Allocated to usual care (n = 175)

12-week follow-up assessment

Completed	(n = 148)
Did not complete	(n = 27)
Died before assessment time	(n = 6)
Hospitalized/hospice	(n = 8)
Transferred care	(n = 4)
Withdrew consent	(n = 5)
Mailed and not returned	(n = 1)
Refused	(n = 2)

12-week follow-up assessment

Completed	(n = 153)
Did not complete	(n = 22)
Died before assessment time	(n = 9)
Hospitalized/hospice	(n = 4)
Transferred care	(n = 3)
Withdrew consent	(n = 1)
Mailed and not returned	(n = 1)
Refused	(n = 4)

24-week follow-up assessment

Completed	(n = 118)
Did not complete	(n = 57)
Died before assessment time	(n = 27)
Hospitalized/hospice	(n = 8)
Transferred care	(n = 9)
Withdrew consent	(n = 7)
Mailed and not returned	(n = 1)
Refused	(n = 5)

24-week follow-up assessment

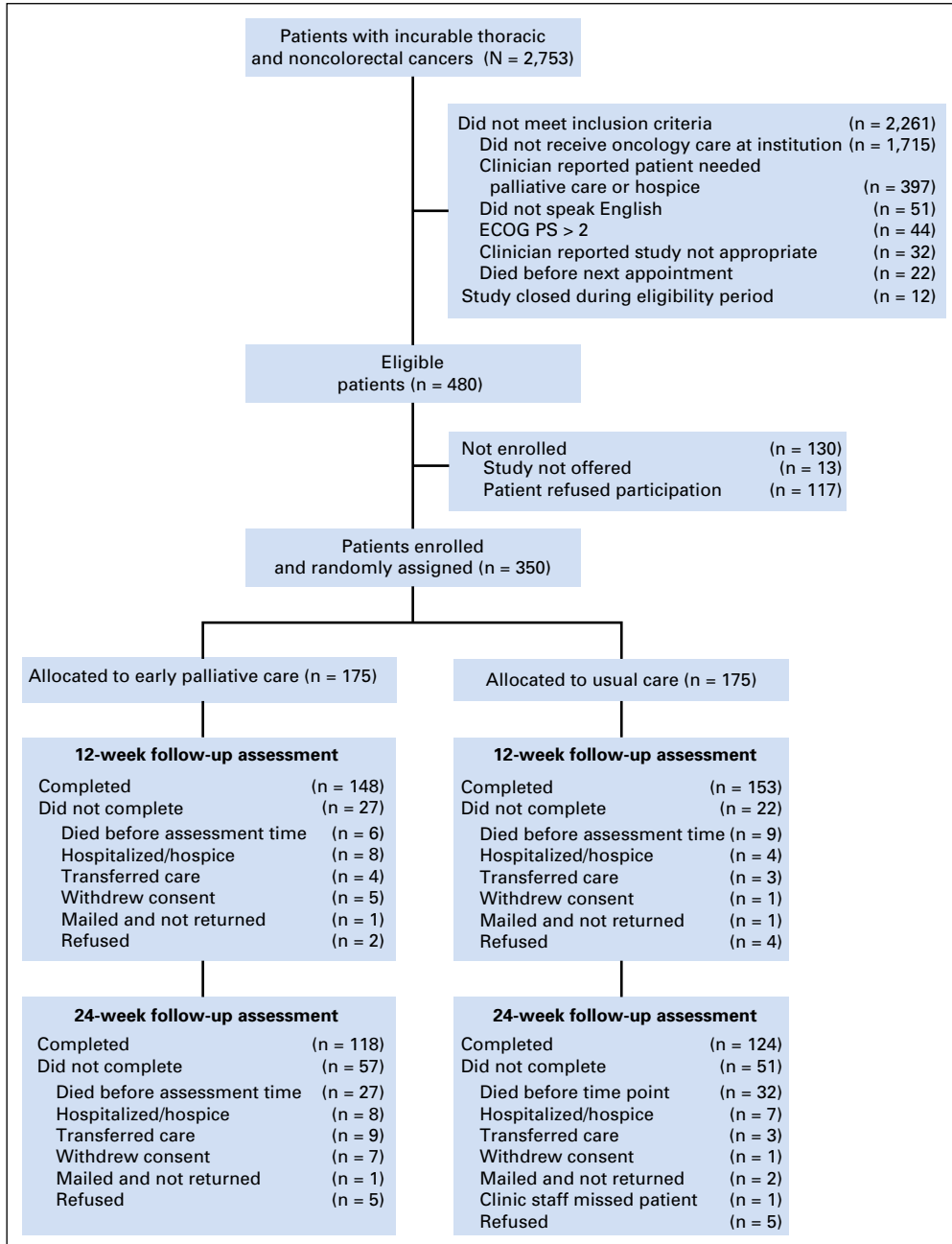|	
Completed	(n = 124)
Did not complete	(n = 51)
Died before time point	(n = 32)
Hospitalized/hospice	(n = 7)
Transferred care	(n = 3)
Withdrew consent	(n = 1)
Mailed and not returned	(n = 2)
Clinic staff missed patient	(n = 1)
Refused	(n = 5)

Fig. A1. CONSORT diagram. ECOG PS, Eastern Cooperative Oncology Group performance status.

Table A1. Demographic and Clinical Characteristics of Lung and GI Cancer Cohorts

Characteristic	Lung Cancer (n = 191) No. (%)	GI Cancer (n = 159) No. (%)	P
Mean age, year (SD)	64.77 (10.67)	64.91 (11.16)	.90
Male	90 (47.1)	99 (62.3)	.005
White	178 (93.19)	145 (91.19)	.485
Marital status			.427
Married	131 (68.59)	114 (71.70)	
Single	19 (9.95)	15 (9.43)	
Divorced	24 (12.57)	12 (7.55)	
Widowed	17 (8.90)	18 (11.32)	
Education			.071
High school or less	81 (42.41)	50 (31.45)	
Some or completed college	76 (39.79)	69 (43.40)	
Graduate school	34 (17.80)	40 (25.16)	
ECOG PS			.320
0	42 (21.99)	46 (28.93)	
1	132 (69.11)	99 (62.26)	
2	17 (8.90)	14 (8.81)	
Charlson Comorbidity Index score, mean (SD)	6.95 (1.37)	6.79 (1.37)	.277
Baseline patient-reported outcomes, mean (SD)			
FACT-G score	78.10 (15.27)	78.57 (15.09)	.772
HADS-Depression score	4.57 (4.09)	4.74 (3.91)	.704
HADS-Anxiety score	5.54 (4.00)	5.03 (3.82)	.231
PHQ-9 score	6.46 (5.58)	6.42 (5.04)	.938
No. of PC visits for those assigned to intervention, mean (SD)			
By week 12	1.98 (2.07)	2.36 (2.29)	.110
By week 24	3.40 (3.39)	4.07 (3.76)	.083
Cancer progression			
Between baseline and week 12	37 (19.37%)	35 (22.01%)	.543
Between weeks 12 and 24	27 (14.14%)	34 (21.38%)	.075
No. of health care use by week 24, mean (SD)			
Hospitalizations	1.97 (1.73)	2.51 (2.44)	.038
Emergency room visits	1.56 (1.66)	1.78 (2.02)	.347

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; FACT-G, Functional Assessment of Cancer Therapy-General scale; HADS, Hospital Anxiety and Depression Scale; PHQ-9, Patient Health Questionnaire-9; SD, standard deviation.