Role of Patient Coping Strategies in Understanding the Effects of Early Palliative Care on Quality of Life and Mood

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ABSTRACT

Purpose

The early integration of oncology and palliative care (EIPC) improves quality of life (QOL) and mood for patients with advanced cancer. However, the mechanisms by which EIPC benefits these outcomes remain unclear. We therefore examined whether EIPC improved patients' coping strategies and if changes in coping accounted for intervention effects on QOL and depressive symptoms.

Patients and Methods

For this secondary analysis of an EIPC trial, we examined data from 350 patients with newly diagnosed incurable lung or GI cancer. Participants completed assessments of QOL (Functional Assessment of Cancer Therapy–General), depressive symptoms (Patient Health Questionnaire–9), and coping (Brief COPE) at baseline and 24 weeks. We used linear regression to test intervention effects on use of coping strategies and mediation regression models with bias-corrected bootstrapping to examine whether improvements in coping mediated the effects of early palliative care on patient-reported outcomes.

Results

Compared with usual oncology care, EIPC significantly increased patient use of approach-oriented coping strategies ($B = 1.09$; $SE = 0.44$; $P = .01$) and slightly reduced use of avoidant strategies ($B = -0.44$; $SE = 0.23$; $P = .06$) from baseline to 24 weeks. Also, the increased use of approach-oriented coping and reduction in avoidant coping were associated with higher QOL and lower depressive symptoms at 24 weeks. The positive changes in approach-oriented coping, but not avoidant coping, significantly mediated the effects of EIPC on QOL (indirect effect, 1.27; 95% CI, 0.33 to 2.86) and depressive symptoms (indirect effect, -0.39 ; 95% CI, -0.87 to -0.08).

Conclusion

Patients with incurable cancer who received EIPC showed increased use of approach-oriented coping, which was associated with higher QOL and reduced depressive symptoms. Palliative care may improve these outcomes by providing patients with the skills to cope effectively with life-threatening illness.

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INTRODUCTION

Patients with incurable cancer experience high symptom burden, often presenting with fatigue, pain, and reduced appetite.¹ Their trajectory is also marked by substantial psychological distress given the poor prognosis, difficult medical decisions, and challenging end-of-life discussions.²⁻⁴ Not surprisingly, depressive and anxiety symptoms are common and associated with worse quality of life (QOL) in this population.⁵ The delivery of palliative care (PC) early in the course of disease represents an innovative model

for addressing the complex supportive care needs of these patients, with burgeoning evidence for its efficacy in improving QOL, mood, and end-of-life care.⁶⁻⁸ The American Society of Clinical Oncology clinical practice guidelines advocate for the integration of PC with standard oncology care, concurrent with active treatment, for those with advanced cancer.⁹

PC clinicians aim to relieve symptom burden and improve QOL by providing specialized knowledge and skills; assessing and treating physical symptoms; ensuring psychosocial, spiritual, and bereavement support; facilitating communication about illness and prognosis with

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Appendix
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patients, family caregivers, and clinicians; and coordinating services and resources.¹⁰⁻¹² Work by our group showed that patients with incurable cancer who received early integrated PC (EIPC) not only reported improved QOL and lower depressive symptoms but also were more likely to discuss wishes for end-of-life care compared with those receiving standard oncology care alone.⁸ Although numerous trials have demonstrated many benefits of EIPC for patients with incurable cancer,^{7,8,13-16} the key mechanisms by which this intervention model leads to improvements in outcomes are not understood. One possible pathway is that PC clinicians provide patients with skills to cope effectively with their life-threatening illness.¹⁷ We therefore hypothesized that EIPC would positively affect the use of coping strategies in patients with incurable cancer. Moreover, we explored whether improvement in coping strategies would mediate the benefits of EIPC with regard to QOL and depressive symptoms.

PATIENTS AND METHODS

Study Design

From May 2011 to July 2015, we recruited patients with newly diagnosed incurable lung or noncolorectal GI cancer from outpatient clinics at the Massachusetts General Hospital (MGH) Cancer Center in Boston, MA, and invited them to participate in a nonblinded, randomized clinical trial of EIPC with oncology care compared with usual oncology care alone. The study was approved by the Dana-Farber/Harvard Cancer Center institutional review board.

Participants

Eligible patients were required to be adults (age > 18 years) within 8 weeks of a diagnosis of incurable lung cancer (non-small cell, small cell, or mesothelioma) or noncolorectal GI cancer (pancreatic, esophageal, gastric, or hepatobiliary) with no history of treatment for metastatic disease; be receiving care at the MGH Cancer Center; have an Eastern Cooperative Oncology Group performance status of 0 to 2; and be able to read and respond to questions in English or do so with minimal interpreter assistance. We did not enroll patients who were already receiving PC services, needed immediate referral for PC or hospice, or had a significant psychiatric or other disease that would interfere with participation.

Procedures

Using the electronic health record, study staff identified potentially eligible patients from the outpatient thoracic and GI oncology clinics and notified oncologists, who invited these patients to participate in the study. After providing informed consent, enrolled participants were randomly assigned to receive EIPC or usual oncology care alone. The MGH Office of Data Quality used a computer-generated number sequence to randomly assign patients in a one-to-one manner, stratified by cancer type. Participants completed self-report assessments at baseline (before random assignment), 12 weeks, and 24 weeks on paper or via Research Electronic Data Capture, a Health Insurance Portability and Accountability Act-compliant Web-based survey tool.

The full trial and intervention procedures have been reported previously.⁸ Patients assigned to EIPC met with a board-certified PC physician or advanced-practice nurse within 4 weeks of enrollment and at least monthly until death, with the option for additional visits. Study visits focused on building rapport, managing symptoms, enhancing coping, improving understanding of illness and prognosis, assisting with treatment decisions, advance care planning, and preparing for the end of life.⁸ Patients assigned to usual oncology care met with a PC clinician only at the

Table 1. Baseline Demographic and Clinical Characteristics

Characteristic	No. (%)	
	Usual Care (n = 175)	Early Palliative Care (n = 175)
Age, years		
Mean	64.03	65.64
SD	10.46	11.26
Male sex	98 (56.0)	91 (52.0)
Race		
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)
Other	1 (0.6)	4 (2.3)
Hispanic/Latino ethnicity	2 (1.1)	7 (4.0)
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/partner	124 (70.9)	121 (69.1)
Single	17 (9.7)	17 (9.7)
Divorced/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/< 10 pack-years	67 (38.3)	75 (42.9)
Current/former smoker	95 (54.3)	93 (53.1)
Unknown	13 (7.4)	7 (4.0)
ECOG performance status		
0	43 (24.6)	45 (25.7)
1	115 (65.7)	116 (66.3)
2	17 (9.7)	14 (8.0)
CCI		
Mean	6.73	7.03
SD	1.39	1.35
FACT-G		
Mean	77.79	78.84
SD	15.46	14.90
PHQ-9		
Mean	6.50	6.39
SD	5.19	5.49
Approach-oriented coping factor (n = 332)		
Mean	18.72	19.01
SD	3.84	3.74
Avoidant coping factor (n = 344)		
Mean	5.98	5.87
SD	2.33	2.28

Abbreviations: CCI, Charlson comorbidity index; ECOG, Eastern Cooperative Oncology Group; FACT-G, Functional Assessment of Cancer Therapy-General; GE, gastroesophageal; PHQ-9, Patient Health Questionnaire-9; SD, standard deviation.

Fig 1. Early palliative care intervention effects on quality of life (QOL) mediated by coping strategies. FACT-G, Functional Assessment of Cancer Therapy–General.

request of the oncologist, patient, or family. Regardless of group assignment, all participants received standard oncology care.

Measures

Sociodemographic and clinical characteristics. Participants reported their race, ethnicity, religion, marital status, smoking history, income, and education level on a demographic questionnaire. Research staff collected data from the electronic health record on patient age, sex, cancer diagnosis, cancer treatment, Charlson comorbidity index (CCI), and Eastern Cooperative Oncology Group performance status.

Coping strategies. We administered selected subscales from the Brief COPE to measure participants' use of coping strategies.¹⁸ The original Brief COPE consists of 28 items assessing diverse coping methods on 14 subscales. To reduce burden, we administered 14 items comprising seven subscales (ie, active coping, use of emotional support, positive reframing, acceptance, behavioral disengagement, denial, and self-blame). Participants rated how often (from "not at all" to "a lot") they had used each strategy to cope with stress since their cancer diagnosis. Researchers advise creating higher-order factors from among the subscales for analyses,¹⁹ and a higher-order factor analysis in our sample revealed a two-factor solution.²⁰ The first higher-order factor was composed of active coping, positive reframing, and acceptance subscales ($\alpha = 0.757$; Appendix Table A1, online only). We labeled this factor approach-oriented coping because these strategies directly address the problem rather than withdraw from it. The second higher-order factor consisted of denial and self-blame subscales ($\alpha = 0.701$), which we referred to as avoidant coping. A higher score on each factor indicated greater use of those strategies. We computed the change in each coping factor by calculating the difference from baseline to weeks 12 and 24, with positive scores indicating increased use of coping strategies.

QOL. To assess QOL, patients completed the Functional Assessment of Cancer Therapy–General (FACT-G) questionnaire,²¹ a well-validated instrument in samples of patients with cancer that possesses excellent psychometric properties. The FACT-G is composed of four subscales (27 items) that measure physical, social, emotional, and functional well-being in the past week, with higher total scores indicating better QOL.

Depressive symptoms. We used the Patient Health Questionnaire–9 (PHQ-9)²² to assess depressive symptoms per the criteria of the *Diagnostic and Statistical Manual* (fourth edition).²³ Validated for patients with cancer,²⁴ the PHQ-9 consists of nine questions about the frequency of depressive symptoms over the past 2 weeks. Total severity score ranges from 0 to 27, with a higher score indicating worse depressive symptoms.

Statistical Analysis

Using the Statistical Package for the Social Sciences (version 22.0; SPSS, Chicago, IL), we described participant sociodemographic and clinical characteristics with measures of central tendency. With all available cases, we calculated linear regression models to examine the effect of group assignment (EIPC v usual care) on change in the two coping factors (approach oriented and avoidant) from baseline to weeks 12 and 24. We adjusted these models for patient age and CCI score given baseline imbalances in these variables between study groups. We then implemented the Preacher and Hayes²⁵ method using the PROCESS²⁵ macro with 5,000-iteration bias-corrected bootstrapping²⁶ to test whether the effects of EIPC on QOL and depressive symptoms at week 24 were mediated through change in approach-oriented and avoidant coping strategies from baseline to week 24.

Using PROCESS, we tested multiple mediation models with group assignment as the independent variable, change in approach-oriented and avoidant coping as mediator variables, and either QOL or depressive symptoms as the dependent variable. We adjusted these models for patient age, CCI, baseline approach-oriented and avoidant coping, and baseline QOL or depressive symptoms. Unstandardized regression coefficients were interpreted on the basis of a two-sided α of 0.05 and evaluated as a measure of effect size.²⁷ Bootstrapped estimates of the specific indirect effects were interpreted with 95% CIs, such that any CIs not containing zero indicated a significant mediation effect. The magnitude of the indirect effect was interpreted as the amount by which QOL or depressive symptoms were expected to increase or decrease indirectly through coping for patients assigned to EIPC versus usual oncology care.²⁸ To determine if the effect of EIPC on coping strategies was clinically meaningful, we examined whether the 95% CI around the mean change in coping strategies overlapped with the null hypothesis (the mean of the control group).²⁹ Also, to address missing data on study outcomes at the 24-week follow-up assessment, we verified findings from the available-case analyses with structural equation modeling in Mplus,³⁰ which uses the full information maximum likelihood method to estimate missing data values from variable relations in the full sample.³¹ Finally, we performed a correction for multiple tests with the false-discovery rate (FDR) control method developed by Benjamini and Hochberg,³² in which each P value is compared with the critical value $[(i/m)Q]$, such that i = the P value rank, m = number of tests, and Q = FDR chosen by researchers. We chose an FDR of 0.20, which represents an acceptable percentage of results in an exploratory study as potential false positives to prevent missing salient findings.^{32,33} The largest P value that is less than the critical value (as well as all smaller P values) is considered significant.

RESULTS

A total of 350 participants were enrolled and randomly assigned to either EIPC ($n = 175$) or usual care ($n = 175$; Appendix Fig A1, online only). A majority of participants were white (92.3%) and male (54.0%), with a sample mean age of 64.84 years (standard deviation, 10.88 years; Table 1). Scores on measures of QOL, depressive symptoms, and coping did not differ between groups at baseline. The two coping factors were inversely correlated with each other at baseline ($r = -0.23$; $P < .001$) and 24 weeks ($r = -0.17$; $P = .01$) but not at 12 weeks ($r = -0.12$; $P = .09$).

EIPC Intervention Effects on Patient Coping Strategies

Linear regression analyses revealed no significant effects of EIPC on change in approach-oriented ($B = 0.42$; $SE = 0.41$;

$P = .31$; 95% CI, -0.39 to 1.23) or avoidant coping strategies ($B = -0.41$; $SE = 0.22$; $P = .07$; 95% CI, -0.85 to 0.03) from baseline to 12 weeks, controlling only for age and CCI. However, compared with the usual oncology care group, patients who received EIPC reported significantly greater use of approach-oriented coping strategies from baseline to 24 weeks ($B = 1.09$; $SE = 0.44$; $P = .01$; 95% CI, 0.23 to 1.96). Specifically, patients in the EIPC group had a mean increase in use of approach-oriented coping ($M = 0.21$; $SE = 0.30$; 95% CI, -0.39 to 0.81) compared with a mean reduction in approach-oriented coping among patients receiving standard oncology care ($M = -0.88$; $SE = 0.31$; 95% CI, -1.50 to -0.27 ; $M_{diff} = 1.09$; $SE_{diff} = 0.44$). Finally, the effect of group assignment on change in avoidant coping from baseline to 24 weeks did not reach significance ($B = -0.44$; $SE = 0.23$; $P = .06$; 95% CI, -0.90 to 0.02).

Table 2. Multiple Mediated Regression: Early Palliative Care Intervention Effects on QOL Mediated by Approach-Oriented and Avoidant Coping ($n = 201$)

Variable	Unstandardized			
	<i>B</i>	SE	<i>P</i>	95% CI
Regression 1: effects on QOL at 24 weeks				
Early palliative care intervention	5.36	1.69	.002	2.04 to 8.69
Age, years	0.0001	0.80	.999	−0.16 to 0.16
CCI	−2.28	0.63	< .001	−3.51 to −1.05
Baseline QOL	0.52	0.06	< .001	0.41 to 0.63
Model summary: QOL (FACT-G)		$R^2 = 0.32$; $F(4,235) = 27.70$; $P = < .001$		
Regression 2a*: effects on mediator 1 (approach-oriented coping Δ)				
Early palliative care intervention	1.16	0.44	.009	0.29 to 2.03
Age, years	−0.02	0.02	.398	−0.06 to 0.02
CCI	−0.11	0.16	.478	−0.43 to 0.20
Baseline QOL	0.05	0.02	.002	0.02 to 0.09
Baseline approach-oriented coping	−0.58	0.07	< .001	−0.72 to −0.45
Baseline avoidant coping	0.10	0.12	.381	−0.13 to 0.33
Model summary: approach-oriented coping Δ		$R^2 = 0.31$; $F(6,194) = 14.19$; $P = < .001$		
Regression 2b*: effects on mediator 2 (avoidant coping Δ)				
Early palliative care intervention	−0.37	0.24	.119	−0.84 to 0.10
Age, years	0.003	0.01	.804	−0.02 to 0.03
CCI	−0.04	0.09	.695	−0.20 to 0.14
Baseline QOL	−0.01	0.009	.186	−0.03 to 0.01
Baseline approach-oriented coping	−0.08	0.04	.031	−0.15 to −0.01
Baseline avoidant coping	−0.55	0.06	< .001	−0.67 to −0.42
Model summary: avoidant coping Δ		$R^2 = 0.30$; $F(6,194) = 13.59$; $P = < .001$		
Regression 3: effects on QOL accounting for mediators 1 and 2 (approach-oriented and avoidant coping Δ)				
Approach-oriented coping Δ (baseline to 24 weeks)	1.10	0.28	< .001	0.55 to 1.64
Avoidant coping Δ (baseline to 24 weeks)	−1.78	0.51	< .001	−2.80 to −0.77
Early palliative care intervention	2.69	1.73	.121	−0.72 to 6.11
Age, years	−0.07	0.08	.368	−0.09 to 0.23
CCI	−2.79	0.61	< .001	−4.0 to −1.58
Baseline QOL	0.43	0.07	< .001	0.29 to 0.56
Baseline approach-oriented coping	0.84	0.31	.007	0.23 to 1.45
Baseline avoidant coping	−0.86	0.53	.105	−1.90 to 0.18
Model summary: QOL (FACT-G)		$R^2 = .44$; $F(8,192) = 18.64$; $P = < .001$		
		Bootstrapped		
	Effect	SE	95% CI	
Indirect effects of palliative care intervention on QOL				
Total effect	1.93†	0.81	0.61 to 3.79	
Indirect effect for approach-oriented coping Δ	1.27†	0.64	0.33 to 2.86	
Indirect effect for avoidant coping Δ	0.66	0.49	−0.02 to 2.00	

Abbreviations: CCI, Charlson comorbidity index; FACT-G, Functional Assessment of Cancer Therapy-General; QOL, quality of life.

*Results of regressions 2a and 2b vary from the simple main effects of the intervention on coping reported in the text because regressions 2a and 2b control for additional covariates (ie, baseline values) within the PROCESS module.

† $P < .05$.

Given that the 95% CI for mean approach-oriented coping strategies in the EIPC group did not overlap with the mean change in approach-oriented coping strategies in the control group and only overlapped slightly with the upper CI for the control group, the benefit that EIPC confers on approach-oriented coping strategies can be considered clinically significant and meaningful. Also, using an acceptable FDR of 20% to correct for multiple tests, the original *P* values for the effect of EIPC on increasing 24-week approach-oriented coping ($P = .01$) and decreasing 24-week avoidant coping ($P = .06$) were smaller than the largest *P* value that was less than the critical value ($P = .09$). Therefore, we can deduce that the effect of EIPC is robust for increasing approach-oriented coping and continues to be less robust for decreasing avoidant coping.

QOL Effects Mediated Through Change in Coping

As previously reported,⁸ group assignment significantly predicted 24-week QOL controlling for age, CCI, and baseline QOL, such that patients who received EIPC had better QOL at week 24 compared with the usual care group (Fig 1). Furthermore, increases in approach-oriented and decreases in avoidant coping were significantly associated with higher QOL at 24 weeks. With both group assignment and changes in approach-oriented and avoidant coping (mediators) simultaneously entered in the regression model, the effect of EIPC on 24-week QOL became nonsignificant (Fig 1).

The full mediation regression model assessing the effect of the EIPC intervention on 24-week QOL mediated by change in approach-oriented and avoidant coping revealed a significant indirect effect through change in approach-oriented coping, such that QOL increased by 1.27 points on the FACT-G indirectly through increased approach-oriented coping for patients assigned to EIPC (Table 2). The indirect effect through decreased avoidant coping was not significant. Overall, the full model accounted for 44% of the variance in QOL, and 42% of the total effect was attributed to the indirect effect (bootstrapped SE = 2.82; 95% CI, 0.13 to 1.54).

Depressive Symptom Effects Mediated Through Change in Coping

As previously reported,⁸ group assignment also significantly predicted 24-week depressive symptoms controlling for age, CCI, and baseline depressive symptoms, such that patients who received EIPC had fewer depressive symptoms at week 24 compared with the usual care group (Fig 2). Furthermore, both increases in approach-oriented coping and decreases in avoidant coping were significantly associated with a reduction in depressive symptoms at week 24. With both group assignment and changes in approach-oriented and avoidant coping (mediators) simultaneously entered in the regression model, the effect of EIPC on depressive symptoms was no longer significant (Fig 2).

The full mediation regression model assessing the effect of the EIPC intervention on depressive symptoms mediated by change in approach-oriented and avoidant coping revealed a significant indirect effect through change in approach-oriented coping, such that patients assigned to EIPC experienced a 0.39-point reduction in depressive symptoms indirectly through increased approach-oriented coping (Table 3). The indirect effect through avoidant coping was not statistically significant. Overall, the full model accounted for 37% of the variance in depressive symptoms, and 63% of the total effect was attributed to the indirect effect (bootstrapped SE = 18.12; 95% CI = -0.93 to 6.08).

Supplemental Analyses

We conducted multiple mediation analyses with the three approach-oriented coping subscales (ie, active coping, positive reframing, and acceptance) entered separately rather than as a higher-order factor to examine their relative indirect effects (Appendix Table A1). Finally, approximately one third of the sample was missing data on 24-week outcomes (FACT-G, 31%; PHQ-9, 32%). Analyses in Mplus with full information maximum likelihood showed that effects on coping were consistent; EIPC predicted increases in approach-oriented coping and decreases in avoidant coping. The indirect effects of EIPC on QOL and depressive symptoms through approach-oriented and avoidant coping were generally consistent, with the exception of

Fig 2. Early palliative care intervention effects on depressive symptoms mediated by coping strategies. PHQ-9, Patient Health Questionnaire-9.

Table 3. Multiple Mediated Regression: Early Palliative Care Intervention Effects on Depressive Symptoms Mediated by Approach-Oriented and Avoidant Coping (n = 201)

Variable	Unstandardized			
	<i>B</i>	SE	<i>P</i>	95% CI
Regression 1: effects on depressive symptoms at 24 weeks				
Early palliative care intervention	−1.17	0.59	.048	−2.33 to −0.10
Age, years	0.02	0.03	.444	−0.03 to 0.08
CCI	0.65	0.22	.003	0.22 to 1.08
Baseline depressive symptoms	0.42	0.06	< .001	0.31 to 0.53
Model summary: depressive symptoms (PHQ-9)	<i>R</i> ² = .23; <i>F</i> (4,234) = 17.87; <i>P</i> = < .001			
Regression 2a*: effects on mediator 1 (approach-oriented coping Δ)				
Early palliative care intervention	1.11	0.45	.014	0.23 to 1.99
Age, years	−0.01	0.02	.511	−0.06 to 0.03
CCI	−0.14	0.16	.378	−0.46 to 0.18
Baseline depressive symptoms	−0.09	0.47	.070	−0.18 to 0.01
Baseline approach-oriented coping	−0.53	0.07	< .001	−0.66 to −0.40
Baseline avoidant coping	0.05	0.12	.664	−0.18 to 0.28
Model summary: approach-oriented coping Δ	<i>R</i> ² = .28; <i>F</i> (6,194) = 12.66; <i>P</i> = < .001			
Regression 2b*: effects on mediator 2 (avoidant coping Δ)				
Early palliative care intervention	−0.37	0.24	.124	−0.83 to 0.10
Age, years	0.002	0.01	.829	−0.02 to 0.02
CCI	−0.03	0.09	.727	−0.20 to 0.14
Baseline depressive symptoms	0.04	0.03	.161	−0.01 to 0.09
Baseline approach-oriented coping	−0.09	0.04	.014	−0.16 to −0.02
Baseline avoidant coping	−0.55	0.06	< .001	−0.67 to −0.42
Model summary: avoid coping Δ	<i>R</i> ² = .30; <i>F</i> (6,194) = 13.64; <i>P</i> = < .001			
Regression 3: effects on depressive symptoms accounting for mediators 1 and 2 (approach-oriented and avoidant coping Δ)				
Approach-oriented coping Δ (baseline to 24 weeks)	−0.35	0.09	< .001	−0.53 to −0.17
Avoidant coping Δ (baseline to 24 weeks)	0.79	0.17	< .001	0.45 to 1.13
Early palliative care intervention	−0.40	0.58	.490	−1.55 to 0.74
Age, years	−0.01	0.03	.820	−0.06 to 0.05
CCI	0.75	0.21	< .001	0.34 to 1.16
Baseline depressive symptoms	0.34	0.06	< .001	0.22 to 0.46
Baseline active coping	−0.24	0.10	.015	−0.44 to −0.05
Baseline avoidant coping	0.37	0.18	.038	0.02 to 0.72
Model summary: depressive symptoms (PHQ-9)	<i>R</i> ² = .37, <i>F</i> (8,192) = 14.00; <i>P</i> = < .001			
			Bootstrapped	
	Effect	SE	95% CI	
Indirect effects of palliative care intervention on depressive symptoms				
Total effect	−0.68†	0.29	−1.36 to −0.21	
Indirect effect for approach-oriented coping Δ	−0.39†	0.20	−0.87 to −0.08	
Indirect effect for avoidant coping Δ	−0.29	0.22	−0.92 to 0.01	

Abbreviations: CCI, Charlson comorbidity index; PHQ-9, Patient Health Questionnaire-9.

*Results of regressions 2a and 2b vary from the simple main effects of the intervention on coping reported in the text because regressions 2a and 2b control for additional covariates (ie, baseline values) within the PROCESS module.

† $P < .05$.

a marginally significant effect of EIPC on depressive symptoms through approach-oriented coping (Appendix Table A2, online only).

DISCUSSION

In this trial of EIPC versus usual oncology care for patients with incurable lung or GI cancer, we observed that the intervention led to greater use of approach-oriented coping over time. Furthermore, these positive changes in patient coping accounted for significant improvements in QOL and depressive symptoms. Thus, this secondary analysis extends the evidence base regarding the benefits of the EIPC model, while also elucidating the mechanisms

by which the intervention affects key patient-reported outcomes. Investigators have increasingly called for studies that specify the processes by which psychosocial interventions improve outcomes for patient with cancer as an essential step in developing and disseminating the most effective interventions.^{34,35}

Our prior qualitative and descriptive work of the EIPC model has shown that PC clinicians consider the enhancement of patient coping efforts to be a primary component of their treatment, in addition to assisting with symptoms, illness understanding, treatment decision making, and planning for end-of-life care.³⁶⁻³⁸ Specifically, PC clinicians commonly engage patients regarding their use of various types of coping strategies, such as behavioral (eg, exercise, hobbies), cognitive (eg, mindfulness, gratitude), spiritual (eg, prayer, pastoral care), and existential (eg, life review,

maintaining hope) coping, as well as referral for counseling and support.³⁹ To our knowledge, this is the first quantitative analysis using a randomized trial design to demonstrate that EIPC can positively shape the coping efforts of patients with incurable cancer over time.

A prior cross-sectional study of patients with incurable cancer showed that coping with use of acceptance is associated with better QOL and mood, whereas denial and self-blame are associated with worse QOL and mood.⁴⁰ Our study confirms and expands upon these findings by demonstrating that changes in approach-oriented coping strategies over time have similar effects. Moreover, the increased use of approach-oriented coping strategies significantly accounted for the positive effects of the EIPC intervention on patient-reported QOL and depressive symptoms. As health care systems strive to increase access to PC services, clarifying the ways by which EIPC improves patient outcomes can greatly inform care delivery. Given the insufficient numbers of PC clinicians to meet the complex supportive care needs of all patients with advanced cancer,⁴¹ these data may guide the development of innovative models for delivering EIPC by highlighting which aspects of treatment require specialty PC expertise versus components that could be delivered through primary or mental health clinicians.

Although our study offers new insights into the relationships of EIPC with patient coping, QOL, and mood, several limitations warrant consideration. As a single-site trial with a specialized PC team and a homogenous sample of patients, the extent to which the findings can be generalized across care settings and to patients with diverse sociodemographic characteristics remains unclear. Furthermore, to reduce burden, we elected not to administer all subscales of the Brief COPE measure, which may have revealed other aspects of coping that account for the changes in outcomes. Knowledge of prior coping styles may also explain use of coping strategies after EIPC. Moreover, because the timing of change in the coping mediators overlapped with the change in outcomes, we were unable to infer causality of whether improved coping led to better QOL and mood or vice versa. Patients receiving EIPC may

have been referred to psychosocial services, contributing to the increase in approach-oriented coping strategies and improvements in outcomes. In future studies, assessment of the family caregivers' role in coping may help tailor PC interventions to enhance coping efforts. Finally, a qualitative study of audio-recorded PC encounters would elucidate the specific communication strategies that PC clinicians use to teach coping skills.

The state of oncology care has seen tremendous advances in precision medicine and targeted therapies; however, patients' supportive care needs have never been greater, and EIPC represents a novel, efficacious approach toward alleviating suffering and improving QOL for those with advanced disease. As the first mediation analysis of the EIPC model to our knowledge, this study provides evidence suggesting that PC clinicians help improve QOL and mood outcomes in patients with incurable cancer in part by enhancing effective coping processes.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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

AUTHOR CONTRIBUTIONS

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Data analysis and interpretation: All authors

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Role of Patient Coping Strategies in Understanding the Effects of Early Palliative Care on Quality of Life and Mood

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Appendix**Table A1.** Multiple Mediation With Individual Approach-Oriented Coping Subscales (active coping, acceptance-oriented coping, and positive reframing) Entered Simultaneously in Same Model

Variable	Effect	Bootstrapped	
		SE	95% CI
Indirect effects of early palliative care intervention on 24-week QOL			
Active coping Δ	−0.04	0.22	−0.64 to 0.32
Acceptance-oriented coping Δ	0.75*	0.52	0.05 to 2.15
Positive reframing Δ	0.77*	0.49	0.07 to 2.12
Indirect effects of early palliative care intervention on 24-week depressive symptoms			
Active coping Δ	−0.01	0.08	−0.22 to 0.12
Acceptance-oriented coping Δ	−0.07	0.11	−0.41 to 0.08
Positive reframing Δ	−0.30*	0.18	−0.78 to −0.03

NOTE. This table details results of multiple mediation of the individual subscales from the Brief COPE that comprise the approach-oriented higher-order factor. One additional subscale (ie, emotional support) loaded negatively on this higher-order factor.²⁰ To facilitate clarity of scoring and interpretation of relationships among study variables, we excluded the emotional subscale from all analyses reported in the manuscript. Analyses adjusted for patient age, Charlson comorbidity index, and baseline values.

Abbreviation: QOL, quality of life.

*Significant indirect effect ($P < .05$).

Table A2. Replication of Analyses Using Full Information Maximum Likelihood in MPlus to Estimate Direct and Indirect Effects With Missing Data (N = 350)

Variable	Unstandardized			
	B	SE	P	95% CI
Main effects of early palliative care intervention on approach-oriented and avoidant coping with estimated missing data				
Direct effect on approach-oriented coping Δ	1.09	0.44	.010*	0.23 to 1.92
Direct effect on avoidant coping Δ	−0.44	0.22	.050	−0.91 to −0.03
Indirect effects of early palliative care intervention on 24-week QOL through approach-oriented and avoidant coping with estimated missing data				
Indirect effect through approach-oriented coping Δ	1.40	0.66	.040*	0.36 to 3.00
Indirect effect through avoidant coping Δ	0.80	0.51	.110	0.08 to 2.18
Indirect effect of early palliative care intervention on 24-week depressive symptoms through approach-oriented and avoidant coping with estimated missing data				
Indirect effect through approach-oriented coping Δ	−0.41	0.21	.050	−0.92 to −0.09
Indirect effect through avoidant coping Δ	−0.39	0.24	.100	−1.10 to −0.04

NOTE. Analyses adjusted for covariates identical to those in the original regression models in [Tables 2](#) and [3](#).

Abbreviation: QOL, quality of life.

* $P < .05$.

Patient Coping Strategies Mediate Early Palliative Care Effects

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