

## JAMA | Original Investigation

# Stepped Palliative Care for Patients With Advanced Lung Cancer

## A Randomized Clinical Trial

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**IMPORTANCE** Despite the evidence for early palliative care improving outcomes, it has not been widely implemented in part due to palliative care workforce limitations.

**OBJECTIVE** To evaluate a stepped-care model to deliver less resource-intensive and more patient-centered palliative care for patients with advanced cancer.

**DESIGN, SETTING, AND PARTICIPANTS** Randomized, nonblinded, noninferiority trial of stepped vs early palliative care conducted between February 12, 2018, and December 15, 2022, at 3 academic medical centers in Boston, Massachusetts, Philadelphia, Pennsylvania, and Durham, North Carolina, among 507 patients who had been diagnosed with advanced lung cancer within the past 12 weeks.

**INTERVENTION** Step 1 of the intervention was an initial palliative care visit within 4 weeks of enrollment and subsequent visits only at the time of a change in cancer treatment or after a hospitalization. During step 1, patients completed a measure of quality of life (QOL; Functional Assessment of Cancer Therapy–Lung [FACT-L]; range, 0–136, with higher scores indicating better QOL) every 6 weeks, and those with a 10-point or greater decrease from baseline were stepped up to meet with the palliative care clinician every 4 weeks (intervention step 2). Patients assigned to early palliative care had palliative care visits every 4 weeks after enrollment.

**MAIN OUTCOMES AND MEASURES** Noninferiority (margin = −4.5) of the effect of stepped vs early palliative care on patient-reported QOL on the FACT-L at week 24.

**RESULTS** The sample (n = 507) mostly included patients with advanced non-small cell lung cancer (78.3%; mean age, 66.5 years; 51.4% female; 84.6% White). The mean number of palliative care visits by week 24 was 2.4 for stepped palliative care and 4.7 for early palliative care (adjusted mean difference, −2.3;  $P < .001$ ). FACT-L scores at week 24 for the stepped palliative care group were noninferior to scores among those receiving early palliative care (adjusted FACT-L mean score, 100.6 vs 97.8, respectively; difference, 2.9; lower 1-sided 95% confidence limit, −0.1;  $P < .001$  for noninferiority). Although the rate of end-of-life care communication was also noninferior between groups, noninferiority was not demonstrated for days in hospice (adjusted mean, 19.5 with stepped palliative care vs 34.6 with early palliative care;  $P = .91$ ).

**CONCLUSIONS AND RELEVANCE** A stepped-care model, with palliative care visits occurring only at key points in patients' cancer trajectories and using a decrement in QOL to trigger more intensive palliative care exposure, resulted in fewer palliative care visits without diminishing the benefits for patients' QOL. While stepped palliative care was associated with fewer days in hospice, it is a more scalable way to deliver early palliative care to enhance patient-reported outcomes.

**TRIAL REGISTRATION** ClinicalTrials.gov Identifier: [NCT03337399](https://clinicaltrials.gov/ct2/show/study/NCT03337399)

JAMA. doi:[10.1001/jama.2024.10398](https://doi.org/10.1001/jama.2024.10398)  
Published online June 2, 2024.

 [Visual Abstract](#)

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More than a decade ago, national guidelines began to recommend delivery of palliative care by specialty-trained clinicians for patients with advanced cancer, either at the time of diagnosis or when their estimated life expectancy is limited.<sup>1,2</sup> These guidelines were based on multiple trials demonstrating the benefits of early palliative care for improving key outcomes in both patients and caregivers, including patient-reported quality of life (QOL) and mood, as well as receipt of high-quality end-of-life care.<sup>3-10</sup> Despite the evidence, this efficacious care model has not been widely implemented, due in part to the shortage of palliative care clinicians, especially in community and limited-resource settings.<sup>11-16</sup> Moreover, in the years since most early palliative care trials were conducted, treatment options for patients with many historically poor-prognosis advanced cancers have expanded, affording patients more effective therapies that prolong survival.<sup>17,18</sup> The lack of palliative care resources and shifting patient needs due to improvements in cancer therapeutics highlight the need for less resource-intensive and more patient-centered palliative care models.<sup>19</sup> Moreover, the historical model of a referral system that relies on oncologists to identify patients with cancer who may benefit from early palliative care remains inadequate.<sup>20,21</sup>

We developed a stepped palliative care intervention based on evidence-based care models that improve access to health care for specialties with an insufficient number of trained clinicians.<sup>22-25</sup> In stepped care, all patients receive care for their condition, but with a minimum of required contact with a specialty-trained clinician. More intensive treatment with the clinician is reserved for patients who do not benefit sufficiently from the less intensive therapies. A key element of this model is that patients must be monitored systematically and “stepped up” to more intensive treatment if less exposure to the clinician does not achieve sufficient benefit. In addition to using fewer resources by requiring minimum contact for patients who do not need more frequent visits, applying a stepped-care model is also a means to deliver more patient-centered care, tailoring palliative care to patients’ clinical needs.

We therefore conducted a multisite trial with a primary aim of examining the noninferiority of stepped vs early palliative care on patient-reported QOL among patients with advanced lung cancer based on the strong evidence base that established early palliative care as the standard of care in this population. We selected a noninferiority margin for QOL based on intervention effects observed in prior studies of early palliative care compared with usual oncology care and below the threshold for a clinically meaningful difference.<sup>5,26,27</sup> Secondary and exploratory outcomes included the impact of the stepped-care model on utilization of palliative care and hospice services and other patient-reported outcomes.

## Methods

### Trial Design and Participants

We conducted a prospective, nonblinded, randomized noninferiority trial of stepped vs early palliative care among

### Key Points

**Question** Is stepped care, with palliative care visits occurring only at key points in patients’ cancer trajectories and using a decrement in quality of life (QOL) to trigger more intensive palliative care, an effective model for delivering palliative care to patients with advanced cancer?

**Findings** In this randomized trial of 507 adults with advanced lung cancer, patients assigned to stepped palliative care had significantly fewer palliative care visits and reported QOL scores at week 24 that were noninferior (adjusted mean, 100.6 vs 97.8;  $P < .001$ ) to the QOL scores of patients assigned to an early palliative care model with monthly visits after diagnosis.

**Meaning** Stepped palliative care is an effective and more scalable means to deliver palliative care to improve QOL for patients with advanced lung cancer.

patients with a new diagnosis of incurable lung cancer at 3 US sites (Massachusetts General Hospital [MGH], Boston; Duke Cancer Institute, Durham, North Carolina; and the University of Pennsylvania, Philadelphia). The institutional review boards at the participating sites approved the protocol. Because this was a minimal-risk supportive care study in an advanced cancer population in which hospitalizations and deaths are expected due to disease worsening and given prior early palliative care trials demonstrating no risk of harm, we did not monitor serious adverse events.<sup>28,29</sup> Thus, the MGH investigative team served as the data monitoring committee to monitor intervention delivery and data collection only. We amended the protocol to increase the sample size to account for missing data and to allow remote consenting and video visits after the onset of the COVID-19 pandemic. The protocol was published previously,<sup>30</sup> and the trial protocol and statistical analysis plan are available in [Supplement 1](#) and [Supplement 2](#).

Eligible patients were adults (aged  $\geq 18$  years) receiving care at a participating site and diagnosed with advanced lung cancer (non-small cell lung cancer; small cell lung cancer) or mesothelioma within the prior 12 weeks that was not being treated with curative intent; had a documented Eastern Cooperative Oncology Group performance status of 0 (fully active with no restrictions) to 2 (unable to work and in bed  $< 50\%$  of the day); and could read and respond to questions in English or Spanish. Patients were not eligible if they were already receiving outpatient palliative care, were enrolled in hospice, or had cognitive or psychiatric conditions prohibiting study consent or participation, as determined by the treating oncologists. Participants were scheduled for study visits for a minimum of 12 months.

Research assistants screened patients presenting to the thoracic oncology clinic by reviewing the electronic health record to determine the cancer diagnosis, stage, and treatment goal. Research assistants obtained permission from the oncology team to approach their patients for study participation. With clinician approval, the research assistants approached patients to review study procedures and obtain consent in person before the COVID-19 pandemic and either

in person or remotely (via telephone) after the start of the pandemic. Spanish-speaking patients provided consent through a Spanish-speaking research assistant or with the assistance of a hospital interpreter. Patients who consented were required to complete baseline self-report measures within 2 weeks of consent to be enrolled in the trial.

### Randomization and Study Procedures

Registered patients were randomized 1:1 using computer-generated block randomization, stratified by study site and lung cancer diagnosis (non-small cell lung cancer vs other). Research staff not affiliated with the protocol conducted randomization centrally at MGH for all sites.

Research assistants informed patients of their group assignment and scheduled the initial palliative care visit within 4 weeks of enrollment. Before the COVID-19 pandemic, palliative care visits were scheduled in person, with phone calls used for missed visits that could not be rescheduled within the protocol-required time frame. After the onset of the pandemic, palliative care visits could be conducted using secure videoconferencing. Participants were permitted to defer and reinstate palliative care visits at their or their clinicians' request. Similarly, participants or their oncology and palliative care clinicians could request more frequent palliative care visits than required per the study protocol. Trained palliative care physicians and advanced practice practitioners ( $n = 34$ ) conducted study visits. To ensure intervention fidelity, clinicians received an intervention guide and underwent comprehensive training in the principles of early palliative care delivery with a 6-hour in-person or recorded training session. Palliative care clinicians cared for patients assigned to both study groups and completed a standardized electronic survey after each study visit to document topics addressed during the encounter, although this survey was optional for telephone calls. Finally, the entire study team met monthly to support participant recruitment, intervention delivery, and data collection.

Patients assigned to early palliative care followed identical study procedures as in our prior trials.<sup>5,26</sup> Specifically, patients were scheduled for palliative care visits every 4 weeks and were seen by the inpatient palliative care team during hospital admissions throughout their study participation.

Patients assigned to stepped palliative care started step 1 of the intervention, which included an initial palliative care visit within 4 weeks of enrollment, with subsequent palliative care visits scheduled only at the time of a change in cancer treatment (due to cancer progression, treatment toxicity, or discontinuation of therapy) or after a hospitalization. Patients in step 1 were not required to be seen by the inpatient palliative care team during hospital admissions. Patients in step 1 completed a QOL measure (Functional Assessment of Cancer Therapy-Lung [FACT-L]; range, 0-136, with higher scores indicating better QOL) every 6 weeks for up to 18 months after enrollment. Those with a 10-point or greater decrease from baseline in their score were stepped up to step 2, in which they were scheduled to meet with the palliative care clinician every 4 weeks (eFigure 1 in Supplement 3) and also were seen by the inpatient palliative care team dur-

ing hospital admissions for the remainder of the study period. A 10-point change in the FACT-L is clinically meaningful and correlates with outcomes such as disease progression.<sup>27</sup>

### Outcomes

Participants completed all study self-reported measures at baseline (including reporting of gender, race, and ethnicity) before randomization and every 12 weeks for a total of 48 weeks, except for the demographic questionnaire and Self-Administered Comorbidity Questionnaire (range, 0-36, with higher scores indicating greater comorbidity), which were administered only at baseline. Self-reported measures were described previously and included a sociodemographic questionnaire and validated measures scored in accordance with published guidelines (eAppendix 1 in Supplement 3).<sup>30-37</sup> Participants could complete self-report measures on paper in person or via mail, electronically, or over the telephone at designated time points with a window of  $\pm 21$  days. Measures that were not publicly available in Spanish were translated forward and backward by a Spanish-speaking clinician.

The primary outcome was patient QOL on the FACT-L. Secondary outcomes included (1) palliative care utilization, as measured by the number of palliative care visits; (2) patient-reported communication about end-of-life care preferences, as measured by an item on the Prognosis and Treatment Perceptions Questionnaire (PTPQ), scored dichotomously; and (3) length of stay in hospice, as measured from the date of hospice enrollment until death among patients who died.

There were 3 exploratory outcomes. Depression symptoms were measured by the Patient Health Questionnaire 9, with a range of 0 to 27 and higher scores indicating worse depression. Use of coping strategies were measured by the Brief Coping Orientation to Problems Experienced Inventory, including scales for approach-oriented coping (range, 6-24) and avoidant coping (range, 4-16), with higher scores indicating greater use of each strategy. Perception of prognosis and goal of therapy were measured by 2 items on the PTPQ, scored dichotomously.

### Statistical Analyses

We designed the study to demonstrate the noninferiority of stepped vs early palliative care with a margin of  $-4.5$  points on the FACT-L at week 24.<sup>26</sup> This margin is a little more than half the QOL benefit we observed in our prior trial of early palliative care vs standard care in patients with advanced lung cancer on the FACT-L (7.5 points) and is also below the established threshold of a clinically meaningful difference on this measure (6 points).<sup>26,27</sup> A sample size of 188 patients per group would achieve 80% power to detect noninferiority based on a 1-sided 5% significance level  $t$  test against the margin of  $-4.5$  points, assuming a standard deviation of 17.5 points and an actual mean difference of zero.<sup>26,38</sup> Given an anticipated 36% rate of missing data at week 24 due to loss to follow-up, withdrawal, or death, we planned to enroll 255 per group.

All regression models included main effects for intervention group and randomization stratification factors (study site

and lung cancer type); additional terms are specified below. We report model-based estimates of within-group adjusted means (or proportions) with standard errors and between-group differences with either lower 1-sided 95% confidence limits for noninferiority analyses (which corresponds to the primary 1-sided 5% significance level test for noninferiority)<sup>39</sup> or 2-sided 95% confidence intervals for superiority analyses. Primary comparisons of patient-reported outcomes were made among participants who survived through week 24 (ie, a survivors analysis), given that this was the comparison of primary scientific interest and similar death rates were anticipated across groups.<sup>40,41</sup>

The primary outcome was patient-reported QOL at week 24, measured by FACT-L. The difference in week 24 means between groups was estimated using a linear regression model adjusted for baseline FACT-L score. Noninferiority of stepped palliative care was established if the lower 1-sided 95% confidence limit for the estimated difference in means was greater than the prespecified margin of -4.5 points, which corresponds to the 1-sided 5% significance level test against this margin.<sup>39</sup>

We used a false discovery rate control approach to interpret the results of significance tests of the 3 secondary outcomes with a false discovery rate of 0.15.<sup>42,43</sup> The difference between groups in the mean number of outpatient palliative care visits per patient by week 24 was assessed using linear regression and a 2-sided superiority test. Noninferiority of stepped palliative care in the proportion reporting patient-clinician communication about end-of-life care at each patient's final follow-up assessment was evaluated using a binomial generalized linear model with identity link and a 1-sided test against the prespecified margin of -10%. Among patients who died, noninferiority of stepped palliative care in the mean length of stay in hospice was assessed using linear regression and a 1-sided test against the prespecified margin of -7 days, based on published quality metrics.<sup>44-46</sup>

Exploratory outcomes included patient-reported prognostic understanding, depression symptoms, and coping strategies at week 24. Proportions with prognostic understanding based on PTPQ items eliciting patients' goals of cancer care ("to cure my cancer" vs any other option) and patients' assessment of curability (yes vs no) were compared using binomial generalized linear models with identity link. Patient-reported depression symptoms (assessed by the Patient Health Questionnaire 9) and coping strategies (assessed by the Brief Coping Orientation to Problems Experienced Inventory) at week 24 were compared using linear regression models adjusted for baseline outcome scores. Exploratory outcomes are reported as estimates with 2-sided 95% CIs and are not adjusted for multiple comparisons.

Our primary analysis excluded participants with missing FACT-L scores at week 24. Sensitivity analyses incorporating additional longitudinal data and using multiple imputation for nonresponse (but not truncation due to death) were conducted to evaluate the impact of missing data on results for the primary outcome (eAppendix 2 in [Supplement 3](#)). All analyses used SAS version 9.4 (SAS Institute Inc) or R version 4.3.2 (R Core Team).

## Results

### Patient Participants

Between February 12, 2018, and December 15, 2022, 510 patients were randomized to stepped palliative care (n = 250) or early palliative care (n = 257); 3 patients were deemed ineligible after enrollment ([Figure 1](#)). At 24 weeks, 291 (73.9% of eligible) participants completed the FACT-L. Rates of FACT-L completion at weeks 36 and 48 are shown in [eTable 1](#) in [Supplement 3](#). As shown in [Table 1](#), participants' mean age was 66.5 years, and 260 (51.4%) were women. Fifty-seven participants (11.3%) self-identified as African American or Black and 427 (84.6%) as White. Most participants had non-small cell lung cancer (78.3%) and an Eastern Cooperative Oncology Group performance status of 1 or 2 (75.3%) and were married/partnered (65.7%). Study groups were generally balanced with respect to clinical characteristics. Baseline characteristics of participants who did vs did not complete the FACT-L at week 24 are shown in [eTable 2](#) in [Supplement 3](#).

### Intervention Delivery

[eTable 3](#) in [Supplement 3](#) shows the proportions of eligible patients in the stepped palliative care group (alive and not hospitalized or in hospice) in step 1 of the intervention who completed the FACT-L at each 6-week interval to determine whether they needed to move to step 2. Sixty-six patients (26.4%) assigned to stepped palliative care were stepped up to step 2 by 24 weeks at a median of 70 days, and 91 (36.4%) were stepped up to step 2 by 48 weeks. Palliative care clinicians completed the survey documenting the visit content for 1180 of 1251 (94.3%) and 1812 of 1927 (94.0%) face-to-face visits by weeks 24 and 48, respectively. Intervention fidelity by study group assignment up to weeks 24 and 48 is shown in [eFigure 2](#) in [Supplement 3](#).

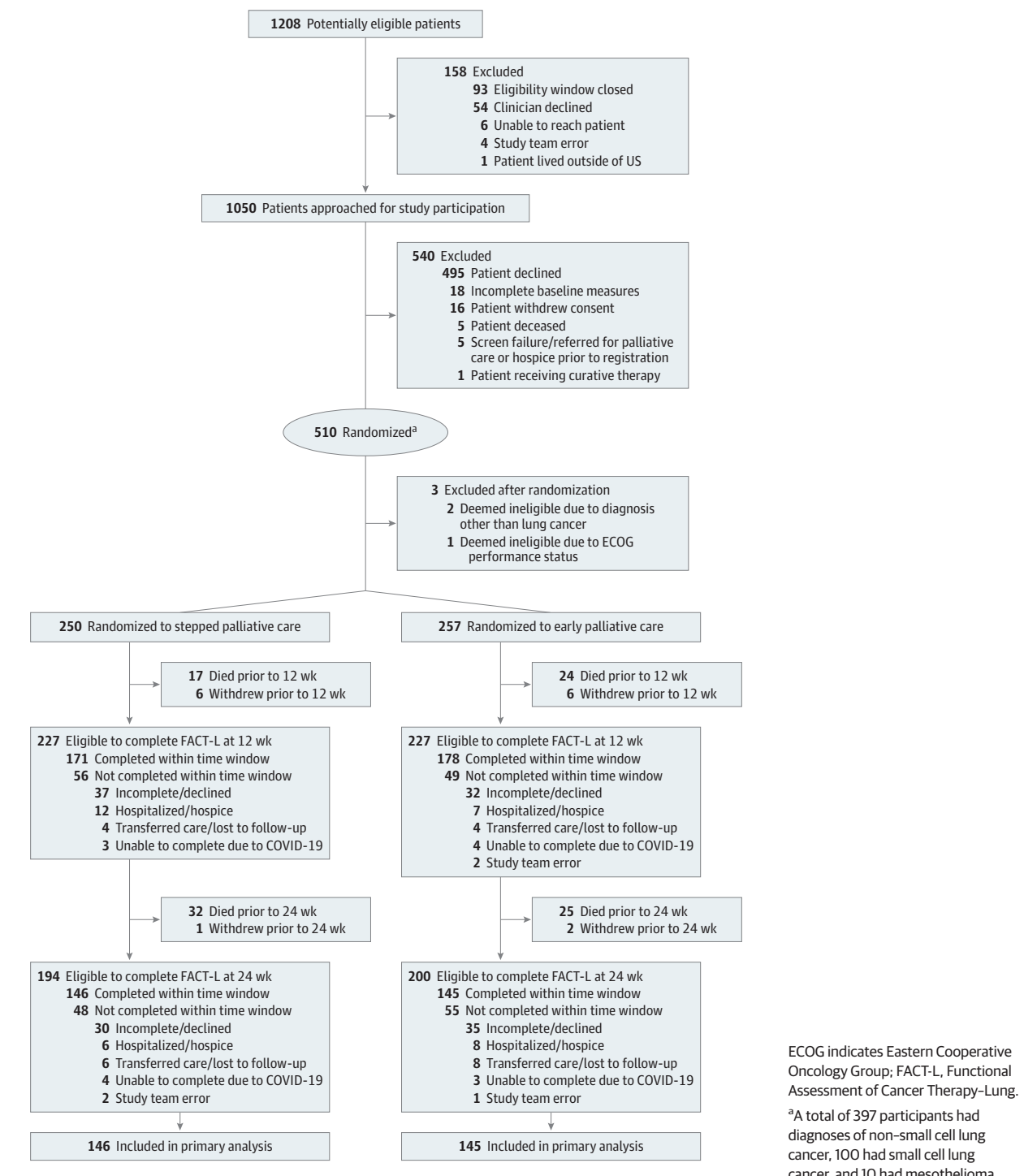
### Primary Outcome

Quality-of-life scores on the FACT-L at week 24 for patients assigned to stepped palliative care were noninferior to those assigned to early palliative care (adjusted mean score, 100.6 vs 97.8; difference, 2.9; lower 1-sided 95% confidence limit, -0.1;  $P < .001$ ) ([Table 2](#) and [Figure 2](#)). In accordance with a more stringent 1-sided 2.5% significance level test for noninferiority, we also calculated a post hoc lower 1-sided 97.5% confidence limit for the primary QOL outcome (difference, 2.9; lower 1-sided 97.5% confidence limit, -0.7), which also supported noninferiority of stepped palliative care. [Figure 3A](#) shows the distribution of FACT-L scores up to week 24 by study group, and [eFigure 3](#) in [Supplement 3](#) shows score distribution up to week 48. Sensitivity analyses assessing the impact of missing data supported noninferiority of stepped palliative care ([Figure 2](#); [eTable 4](#) in [Supplement 3](#)).

### Secondary Outcomes

The mean number of palliative care visits by week 24 for patients assigned to stepped palliative care was significantly lower than for those assigned to early palliative care (2.4 vs 4.7 visits; adjusted mean difference, -2.3; 95% CI, -2.7 to -1.8;

**Figure 1. Flow of Participants Through a Trial of Stepped vs Early Palliative Care for Patient With Advanced Lung Cancer**



$P < .001$ ) (Table 2). The mean number of visits by week 48 was also lower for those assigned to stepped palliative care (3.8 vs 7.7 visits; adjusted mean difference,  $-3.9$ ; 95% CI,  $-4.7$  to  $-3.1$ ). Twenty-seven patients assigned to early palliative care and 11 assigned to stepped palliative care had no palliative care visits, primarily due to death, withdrawal, or transfer of care.

The proportion of patients assigned to stepped palliative care who reported discussing their end-of-life care preferences was noninferior to those in the early palliative care group (adjusted proportion, 30.4% vs 33.0%; difference,  $-2.6\%$ ; lower 1-sided 95% confidence limit,  $-10.4\%$ ;  $P = .09$ ). Among deceased participants, 115 of 160 (71.9%) patients in the stepped



Table 1. Baseline Participant Characteristics

Characteristics	Stepped palliative care (n = 250)	Early integrated palliative care (n = 257)
Age, mean (SD), y	66.8 (9.2)	66.1 (11.1)
No. (%) >75	43 (17.2)	58 (22.6)
Women, No./total (%) <sup>a</sup>	130/250 (52.0)	130/256 (50.8)
Race, No. (%) <sup>b</sup>	n = 250	n = 255
African American or Black	29 (11.6)	28 (11.0)
American Indian or Alaska Native	2 (0.8)	2 (0.8)
Asian	3 (1.2)	5 (2.0)
Native Hawaiian or Pacific Islander	0	0
White	215 (86.0)	212 (83.1)
Other <sup>c</sup>	3 (1.2)	5 (2.0)
Hispanic or Latino ethnicity, No./total (%)	3/243 (1.2)	5/250 (2.0)
Religion, No. (%)	n = 246	n = 249
Catholic	98 (39.8)	91 (36.5)
Other Christian (eg, Protestant)	97 (39.4)	106 (42.6)
Jewish	15 (6.1)	13 (5.2)
Atheist	0	3 (1.2)
Muslim	0	2 (0.8)
None	24 (9.8)	28 (11.2)
Other	12 (4.9)	6 (2.4)
Relationship status, No. (%)	n = 247	n = 252
Married/partnered	152 (61.5)	176 (69.8)
Divorced/separated	48 (19.4)	25 (9.9)
Widowed/loss of partner	30 (12.1)	34 (13.5)
Single	17 (6.9)	17 (6.7)
Education, No. (%)	n = 244	n = 248
High school graduate or lower	80 (32.8)	78 (31.5)
Associate degree/technical school	66 (27.0)	59 (23.8)
College degree	52 (21.3)	55 (22.2)
Master's, professional, or doctoral degree	46 (18.9)	56 (22.6)
Annual income, No. (%), \$	n = 221	n = 225
<25 000	42 (19.0)	38 (16.9)
25 000-49 999	49 (22.2)	52 (23.1)
50 000-99 999	63 (28.5)	56 (24.9)
100 000-149 999	27 (12.2)	33 (14.7)
≥150 000	40 (18.1)	46 (20.4)
Smoking status, No. (%)	n = 232	n = 228
Current or former	168 (72.4)	146 (64.0)
Never or <10 pack-years	64 (27.6)	82 (36.0)
Cancer type, No. (%)		
Non-small cell lung cancer	194 (77.6)	203 (79.0)
Small cell lung cancer	53 (21.2)	47 (18.3)
Mesothelioma	3 (1.2)	7 (2.7)
Cancer treatment, No. (%)		
Platinum-based doublet chemotherapy	128 (51.2)	116 (45.1)
Radiation	54 (21.6)	38 (14.8)
Oral targeted chemotherapy	40 (16.0)	50 (19.5)
Immunotherapy	22 (8.8)	39 (15.2)
Single-agent intravenous chemotherapy	3 (1.2)	9 (3.5)
No treatment	2 (0.8)	4 (1.6)
Combined radiation and chemotherapy	0	1 (0.4)
Other treatment	1 (0.4)	0

(continued)

Table 1. Baseline Participant Characteristics (continued)

Characteristics	Stepped palliative care (n = 250)	Early integrated palliative care (n = 257)
Cancer gene variant status, No. (%)		
EGFR	37 (14.8)	39 (15.2)
ALK	11 (4.4)	10 (3.9)
ROS	3 (1.2)	2 (0.8)
RET	1 (0.4)	2 (0.8)
Other or no gene variant	198 (79.2)	204 (79.4)
Eastern Cooperative Oncology Group performance status, No. (%)		
0 (Fully active with no restrictions)	61 (24.4)	64 (24.9)
1 (Able to do light work)	153 (61.2)	153 (59.5)
2 (Unable to work and in bed <50% of the day)	36 (14.4)	40 (15.6)
Medical comorbidity (SCQ score), mean (SD) <sup>d</sup>	8.6 (4.4) [n = 240]	7.7 (4.0) [n = 247]
Quality of life (FACT-L score), mean (SD) <sup>e</sup>	93.6 (19.4) [n = 250]	95.7 (19.7) [n = 256]
Depression symptoms (PHQ-9 score), mean (SD) <sup>f</sup>	6.6 (5.1) [n = 240]	6.0 (4.9) [n = 246]
Coping skills (Brief COPE score), mean (SD) <sup>g</sup>		
Approach-oriented coping	17.7 (3.9) [n = 216]	18.2 (3.7) [n = 220]
Avoidant coping	6.0 (2.3) [n = 225]	6.4 (2.6) [n = 228]
Perceptions of prognosis, No./total (%)		
Perceives goal of therapy is to cure cancer	80/237 (33.8)	74/235 (31.5)
Perceives cancer is curable	59/218 (27.1)	54/224 (24.1)
End-of-life care communication, No./total (%)	37/232 (15.9)	23/239 (9.6)

<sup>a</sup> Gender was collected by self-report that allowed a single selection from a predetermined list: man, woman, or other/write-in. No participants selected other.

<sup>b</sup> Race was collected by self-report that allowed multiple selections from a predetermined list, including an other/write-in option. Sum of percentages may exceed 100%.

<sup>c</sup> Indicates participant selected other race. See eAppendix 3 in Supplement 3 for itemization.

<sup>d</sup> Self-Administered Comorbidity Questionnaire (SCQ) score range, 0-36, with higher scores indicating greater comorbidity.

<sup>e</sup> Functional Assessment of Cancer Therapy-Lung Scale (FACT-L) score range, 0-136, with higher scores indicating better quality of life; minimum clinically important difference = 6.

<sup>f</sup> Patient Health Questionnaire 9 (PHQ-9) score range, 0-27, with higher scores indicating more significant depression symptoms.

<sup>g</sup> Brief Coping Orientation to Problems Experienced Inventory (Brief COPE) scores: approach-oriented coping score range, 6-24, with higher scores indicating greater use of approach-oriented coping strategies; avoidant coping score range, 4-16, with higher scores indicating greater use of avoidant coping strategies.

palliative care group and 125 of 162 (77.2%) patients in the early palliative care group received hospice services before death, and hospice length of stay was shorter for patients assigned to stepped palliative care (adjusted mean, 19.5 vs 34.6 days; difference, -15.2 days; lower 1-sided 95% confidence limit, -25.1;  $P = .91$  for noninferiority).

### Exploratory Outcomes

The 2 groups did not differ in prognostic understanding at week 24 with respect to the proportion of patients who reported that the goal of therapy was to cure their cancer or who reported that their cancer was curable, as noted in Table 2. Depression symptoms and use of approach-oriented and avoidant coping at week 24 were not different between those assigned to stepped vs early palliative care (Table 2 and Figure 3).

## Discussion

Stepped care is an effective way to deliver early, integrated palliative and oncology care to improve patients' QOL. Patients assigned to stepped palliative care participated in significantly fewer palliative care visits, thus using substantially fewer

palliative care resources, but had noninferior QOL at week 24 compared with patients participating in monthly visits with a palliative care clinician. Compared with patients assigned to early integrated palliative care, those assigned to stepped palliative care had 49.5% fewer palliative care visits through week 24. Notably, other salient patient-reported outcomes, including depression symptoms, coping, prognostic understanding, and end-of-life care communication, were also not different between study groups. In future research, we plan to evaluate the cost-effectiveness of stepped palliative care compared with early palliative care. To our knowledge, this is the first randomized trial to establish the noninferiority of a patient-centered model tailored to a patient's needs by triggering more intensive palliative care services based on patient-reported QOL compared with the efficacious yet resource-intensive early palliative care model.

The stepped-care model ensures that patients are introduced to palliative care at the time of diagnosis but then triages further palliative care delivery based on their illness trajectory and QOL needs. With integration of palliative care early in the illness course, patients are less likely to equate palliative care with hospice or end-of-life care while still being enabled to establish a rapport with a palliative care clinician over

Table 2. Regression Model Estimates of Study Group Effects on 24-Week Outcome Measures

	Estimated mean or proportion (SE) <sup>a</sup>		Difference (lower 1-sided 95% confidence limit) or difference (95% CI) <sup>b</sup>	P value <sup>c</sup>
Outcome measures	Stepped palliative care (n = 250)	Early integrated palliative care (n = 257)		
Primary outcome test of noninferiority				
Quality of life, FACT-L, mean score <sup>d</sup>	100.6 (1.3) [n = 146]	97.8 (1.3) [n = 145]	2.9 (−0.1)	<.001 <sup>e</sup>
Secondary outcome tests of noninferiority				
Discussed end-of-life care with clinician, % <sup>f</sup>	30.4 (3.3) [n = 190]	33.0 (3.4) [n = 187]	−2.6 (−10.4)	.09 <sup>e</sup>
Length of hospice stay, mean, d <sup>g</sup>	19.5 (4.3) [n = 159]	34.6 (4.2) [n = 161]	−15.2 (−25.1)	.91 <sup>e</sup>
Secondary outcome test of superiority				
Palliative care visits, mean No. per patient	2.4 (0.2) [n = 250]	4.7 (0.1) [n = 257]	−2.3 (−2.7 to −1.8)	<.001
Exploratory outcome tests of superiority				
Depression symptoms, PHQ-9, mean score	5.0 (0.3) [n = 139]	5.3 (0.3) [n = 142]	−0.4 (−1.3 to 0.5)	
Coping skills, Brief COPE				
Approach-oriented coping, mean score	17.7 (0.3) [n = 116]	17.5 (0.3) [n = 115]	0.2 (−0.7 to 1.0)	
Avoidant coping, mean score	5.7 (0.2) [n = 126]	5.7 (0.2) [n = 124]	0.0 (−0.5 to 0.5)	
Perceptions of prognosis				
Perceives goal of therapy is to cure cancer, %	27.9 (3.3) [n = 181]	25.6 (3.2) [n = 184]	2.3 (−6.7 to 11.3)	
Perceives cancer is curable, %	22.2 (3.0) [n = 182]	23.8 (3.1) [n = 176]	−1.6 (−10.0 to 6.8)	

Abbreviations: Brief COPE, Brief Coping Orientation to Problems Experienced Inventory; FACT-L, Functional Assessment of Cancer Therapy–Lung; PHQ-9, Patient Health Questionnaire 9.

<sup>a</sup> All estimates are adjusted for study site and cancer type (non-small cell lung cancer vs small cell lung cancer or mesothelioma). Estimates for FACT-L, PHQ-9, and coping skills are additionally adjusted for baseline scores of outcome variable. Numbers in brackets reflect the number of patients in each group whose data were included in the model.

<sup>b</sup> Comparing the lower 1-sided 95% confidence limit with the noninferiority margin corresponds to the primary 1-sided 5% significance level test for

noninferiority. Confidence intervals for secondary and exploratory outcomes are not adjusted for multiple testing.

<sup>c</sup> P values for secondary outcomes are adjusted for multiple testing using the false discovery rate approach. P values are not reported for exploratory outcomes.

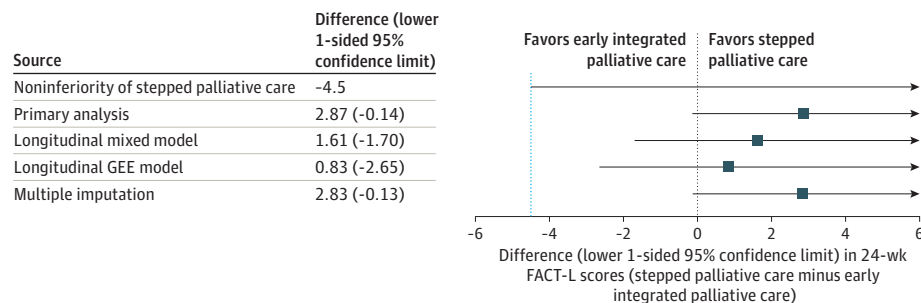
<sup>d</sup> Prespecified noninferiority margin, −4.5 points.

<sup>e</sup> P value for noninferiority.

<sup>f</sup> Prespecified noninferiority margin, −10 percentage points.

<sup>g</sup> Prespecified noninferiority margin, −7 days.

Figure 2. Primary and Sensitivity Analysis Model Estimates of Study Group Effects on the Primary 24-Week Outcome Measure of FACT-L Scores



FACT-L indicates Functional Assessment of Cancer Therapy–Lung; GEE, generalized estimating equation. Points indicate model estimates of the mean between-group difference in FACT-L scores at week 24. All estimates are adjusted for study site and cancer type. Whiskers extend to the lower 1-sided

95% confidence limit for each estimate. Comparing the lower 1-sided 95% confidence limit with the noninferiority margin corresponds to the primary 1-sided 5% significance level test for noninferiority. Sensitivity analysis methods are described in eAppendix 2 in Supplement 3.

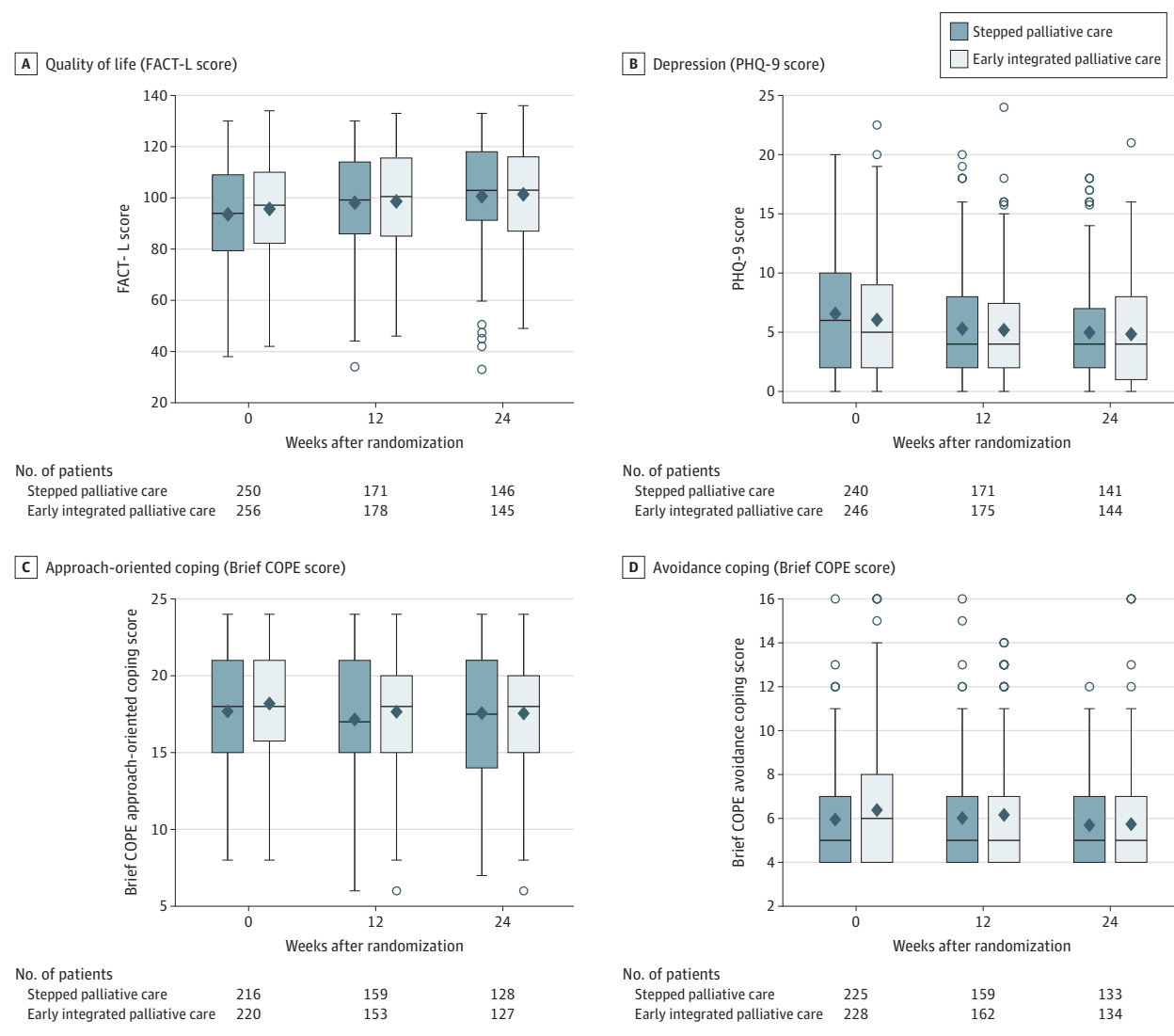
time.<sup>47,48</sup> To ensure continued integration of palliative and oncology care, the stepped-care model entailed visits at key clinical turning points in patients' illness courses. However, many patients who are not hospitalized or experiencing a change in cancer treatment still struggle with living with an incurable illness, so monitoring QOL allows for identification of patients who would benefit from more intensive palliative care.<sup>49,50</sup> Although this model holds promise as a patient-centered strategy to deliver early palliative care using fewer palliative care resources, barriers to implementing it include required moni-

toring of electronic health records for changes in cancer therapy and hospitalizations as well as frequent administration of patient-reported outcomes. However, developing automated queries from electronic health records and more widespread implementation of standard patient-reported outcome measure collection will facilitate using these approaches to deliver palliative care services.<sup>51,52</sup>

Although stepped palliative care was noninferior to early palliative care for QOL, and we detected no differences in patient-reported communication about end-of-life care,



Figure 3. Longitudinal Patient-Reported Outcome Measures Up to 24 Weeks



Brief COPE indicates Brief Coping Orientation to Problems Experienced Inventory; FACT-L, Functional Assessment of Cancer Therapy-Lung; PHQ-9, Patient Health Questionnaire 9. On the box plots, the tops and bottoms of the boxes indicate IQRs; center horizontal lines, medians; and diamonds, means.

Whiskers extend to the highest and lowest values within 1.5 times the IQR, and dots beyond the whiskers reflect outlying data. The numbers beneath the box plots show the number of patients in each group who completed the patient-reported assessment.

hospice length of stay was significantly shorter with stepped palliative care vs early palliative care. Thus, although both groups did meet quality metrics for length of stay in hospice on average (ie, >7 days), more frequent contact with palliative care, especially in the months before death, may facilitate earlier referrals for hospice.<sup>53,54</sup> However, because patients with metastatic cancer, including lung cancer, are living longer, early palliative care starting at the time of diagnosis may no longer be a feasible model to ensure the delivery of high-quality care at the end of life. Integrating additional methods of prognostication, such as predictive modeling to identify patients at risk of death, with novel palliative care delivery models, such as stepped palliative care, warrants further investigation.<sup>55</sup>

### Limitations

This study had several notable limitations. First, although the overall sample was representative of the US population with respect to the proportion of Black participants, few patients self-identified as other than Black or White or as Hispanic or Latino. While our study protocol included procedures for enrolling Spanish-speaking participants and patient-reported outcomes were available in Spanish, additional strategies are needed to ensure an ethnically diverse study sample. Second, as the participating institutions needed to have a sufficient palliative care clinician workforce to deliver monthly palliative care services to study participants, we conducted this trial at 3 academic medical centers that are likely not representative of the community settings where most patients with

cancer receive health care. Our study sample included only patients with advanced lung cancer and mesothelioma, and therefore, the generalizability of the findings to patients diagnosed with other advanced cancers, including those with more indolent disease, requires further investigation. Third, while the eligibility criteria in the current study were similar to our single-site palliative care trials in patients with advanced lung cancer, our rate of missing data was slightly higher than in prior trials, likely due to the heterogeneity of the population and cancer care practices when enrolling patients at multiple sites. The COVID-19 pandemic also likely contributed to participant non-response by leading to delays in cancer diagnoses and challenges with in-person data collection.<sup>56,57</sup> The higher rate of missing data may have reduced the precision of our outcome estimates and potentially introduced bias. Fourth, during and after the COVID-19 pandemic, palliative care visits were permitted via secure video despite a lack of available data dem-

onstrating that video-delivered palliative care is equivalent to in-person palliative care.

## Conclusions

In conclusion, stepped palliative care holds considerable promise to increase the scalability of integrated palliative and oncology care by maintaining the effect of early palliative care on patients' QOL and other salient patient-reported outcomes with fewer palliative care visits. As patients with metastatic cancers are living longer due to improvements in cancer therapeutics, they may have different palliative care needs while living with their cancer vs at the end of life. Identifying additional triggers to intensify palliative care near death is a potential next step to further optimize the stepped palliative care model.

### ARTICLE INFORMATION

**Accepted for Publication:** May 15, 2024.

**Published Online:** June 2, 2024.

doi:10.1001/jama.2024.10398

**Author Contributions:** Dr Temel, Dr Rabideau, Ms Horick, and Dr Greer had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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**Supervision:** Jackson, Rinaldi, Kumar, McGrath, LeBlanc, Jones, Greer.

**Conflict of Interest Disclosures:** Dr Jackson reported receipt of personal fees and equity from Tuesday Health. Dr El-Jawahri reported receipt of personal fees from Incyte, GSK, AIM Pathways, Novartis, and Tuesday Health. Dr LeBlanc reported receipt of grants from AbbVie/Genentech, BMS/Celgene, Coceptis/Deverra, GSK, Jazz Pharmaceuticals, and AstraZeneca; receipt of personal fees from AbbVie/Genentech, Agios/Servier, Apellis, BMS/Celgene, Gilead, GSK, Lilly, Novartis, Pfizer, Astellas, Incyte, Rigel, UpToDate, DoseTrx, and ThymeCare; and equity interest in DoseTrx and ThymeCare. Dr Post reported receipt of a speaking-related honorarium from Medscape Live. Dr Greer reported receipt of personal fees from BeiGene, funding from Blue Note Therapeutics, and book royalties from Oxford University Press. No other disclosures were reported.

**Funding/Support:** This work was supported by National Cancer Institute grant R01CA215188. Dr Temel is an American Cancer Society Clinical Research Professor. Drs El-Jawahri and LeBlanc are Scholars in Clinical Research for the Leukemia and Lymphoma Society.

**Role of the Funder/Sponsor:** The National Cancer Institute had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication.

**Meeting Presentation:** American Society of Clinical Oncology (ASCO); June 2, 2024; Chicago, Illinois.

**Data Sharing Statement:** See [Supplement 4](#).

### REFERENCES

- 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. *J Clin Oncol*. 2012;30(8):880-887. doi:10.1200/JCO.2011.38.5161
- Levy MH, Smith T, Alvarez-Perez A, et al. Palliative care, version 1.2014: featured updates to the NCCN guidelines. *J Natl Compr Canc Netw*. 2014;12(10):1379-1388. doi:10.6004/jncn.2014.0136
- Rabow MW, Dibble SL, Pantilat SZ, McPhee SJ. The comprehensive care team: a controlled trial of outpatient palliative medicine consultation. *Arch Intern Med*. 2004;164(1):83-91. doi:10.1001/archinte.164.1.83
- 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*. 2009;302(7):741-749. doi:10.1001/jama.2009.1198
- Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med*. 2010;363(8):733-742. doi:10.1056/NEJMoa1000678
- Zimmermann C, Swami N, Krzyzanowska M, et al. Early palliative care for patients with advanced cancer: a cluster-randomised controlled trial. *Lancet*. 2014;383(9930):1721-1730. doi:10.1016/S0140-6736(13)62416-2
- Bakitas MA, Tosteson TD, Li Z, et al. Early versus delayed initiation of concurrent palliative oncology care: patient outcomes in the ENABLE III randomized controlled trial. *J Clin Oncol*. 2015;33(13):1438-1445. doi:10.1200/JCO.2014.58.6362
- Kavalieratos D, Corbelli J, Zhang D, et al. Association between palliative care and patient and caregiver outcomes: a systematic review and meta-analysis. *JAMA*. 2016;316(20):2104-2114. doi:10.1001/jama.2016.16840
- Grudzen CR, Richardson LD, Johnson PN, et al. Emergency department-initiated palliative care in advanced cancer: a randomized clinical trial. *JAMA Oncol*. 2016;2(5):591-598. doi:10.1001/jamaoncol.2015.5252
- Hui D, Bruera E. Integrating palliative care into the trajectory of cancer care. *Nat Rev Clin Oncol*. 2016;13(3):159-171. doi:10.1038/nrclinonc.2015.201
- Hui D, Elsayem A, De la Cruz M, et al. Availability and integration of palliative care at US cancer centers. *JAMA*. 2010;303(11):1054-1061. doi:10.1001/jama.2010.258
- Lupu D. Estimate of current hospice and palliative medicine physician workforce shortage. *J Pain Symptom Manage*. 2010;40(6):899-911. doi:10.1016/j.jpainsymman.2010.07.004
- Lupu D, Quigley L, Mehfood N, Salsberg ES. The growing demand for hospice and palliative medicine physicians: will the supply keep up? *J Pain Symptom Manage*. 2018;55(4):1216-1223. doi:10.1016/j.jpainsymman.2018.01.011
- Kayastha N, LeBlanc TW. Why are we failing to do what works? musings on outpatient palliative care integration in cancer care. *JCO Oncol Pract*. 2022;18(4):255-257. doi:10.1200/OP.21.00794
- Hui D, Kim SH, Kwon JH, et al. Access to palliative care among patients treated at a comprehensive cancer center. *Oncologist*. 2012;17(12):1574-1580. doi:10.1634/theoncologist.2012-0192
- Aldridge MD, Hasselaar J, Garraalda E, et al. Education, implementation, and policy barriers to greater integration of palliative care: a literature review. *Palliat Med*. 2016;30(3):224-239. doi:10.1177/0269216315606645
- Reck M, Rabe KF. Precision diagnosis and treatment for advanced non-small-cell lung cancer. *N Engl J Med*. 2017;377(9):849-861. doi:10.1056/NEJMr1703413

18. Howlader N, Forjaz G, Mooradian MJ, et al. The effect of advances in lung-cancer treatment on population mortality. *N Engl J Med*. 2020;383(7):640-649. doi:10.1056/NEJMoai916623
19. Bekelman DB, Rabin BA, Nowels CT, et al. Barriers and facilitators to scaling up outpatient palliative care. *J Palliat Med*. 2016;19(4):456-459. doi:10.1089/jpm.2015.0280
20. Hui D, Meng YC, Bruera S, et al. Referral criteria for outpatient palliative cancer care: a systematic review. *Oncologist*. 2016;21(7):895-901. doi:10.1634/theoncologist.2016-0006
21. Jordan RI, Allsop MJ, ElMokhallati Y, et al. Duration of palliative care before death in international routine practice: a systematic review and meta-analysis. *BMC Med*. 2020;18(1):368. doi:10.1186/s12916-020-01829-x
22. Bower P, Gilbody S. Stepped care in psychological therapies: access, effectiveness and efficiency. *Br J Psychiatry*. 2005;186:11-17. doi:10.1192/bjp.186.1.11
23. Jakicic JM, Tate DF, Lang W, et al. Effect of a stepped-care intervention approach on weight loss in adults: a randomized clinical trial. *JAMA*. 2012;307(24):2617-2626. doi:10.1001/jama.2012.6866
24. Kroenke K, Krebs EE, Wu J, et al. Telecare collaborative management of chronic pain in primary care: a randomized clinical trial. *JAMA*. 2014;312(3):240-248. doi:10.1001/jama.2014.7689
25. Aspvall K, Andersson E, Melin K, et al. Effect of an internet-delivered stepped-care program vs in-person cognitive behavioral therapy on obsessive-compulsive disorder symptoms in children and adolescents: a randomized clinical trial. *JAMA*. 2021;325(18):1863-1873. doi:10.1001/jama.2021.3839
26. 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. *J Clin Oncol*. 2017;35(8):834-841. doi:10.1200/JCO.2016.70.5046
27. 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. *J Clin Epidemiol*. 2002;55(3):285-295. doi:10.1016/S0895-4356(01)00477-2
28. Baim-Lance A, Ferreira KB, Cohen HJ, et al. Improving the approach to defining, classifying, reporting and monitoring adverse events in seriously ill older adults: recommendations from a multi-stakeholder convening. *J Gen Intern Med*. 2023;38(2):399-405. doi:10.1007/s11606-022-07646-7
29. 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. *J Clin Oncol*. 2017;35(1):96-112. doi:10.1200/JCO.2016.70.1474
30. Post KE, Heuer LB, Kamal AH, et al. Study protocol for a randomised trial evaluating the noninferiority of stepped palliative care versus early integrated palliative care for patients with advanced lung cancer. *BMJ Open*. 2022;12(2):e057591. doi:10.1136/bmjopen-2021-057591
31. Sangha O, Stucki G, Liang MH, et al. The Self-Administered Comorbidity Questionnaire: a new method to assess comorbidity for clinical and health services research. *Arthritis Rheum*. 2003;49(2):156-163. doi:10.1002/art.10993
32. Cella D. The Functional Assessment of Cancer Therapy-Lung and Lung Cancer Subscale assess quality of life and meaningful symptom improvement in lung cancer. *Semin Oncol*. 2004;31(3)(suppl 9):11-15. doi:10.1053/j.seminoncol.2004.04.008
33. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med*. 2001;16(9):606-613. doi:10.1046/j.1525-1497.2001.016009606.x
34. Carver CS. You want to measure coping but your protocol's too long: consider the Brief COPE. *Int J Behav Med*. 1997;4(1):92-100. doi:10.1207/s15327558ijbm0401\_6
35. Hagan TL, Fishbein JN, Nipp RD, et al. Coping in patients with incurable lung and gastrointestinal cancers: a validation study of the Brief COPE. *J Pain Symptom Manage*. 2017;53(1):131-138. doi:10.1016/j.jpainsymman.2016.06.005
36. El-Jawahri A, Traeger L, Park ER, et al. Associations among prognostic understanding, quality of life, and mood in patients with advanced cancer. *Cancer*. 2014;120(2):278-285. doi:10.1002/cncr.28369
37. Wright AA, Zhang B, Ray A, et al. Associations between end-of-life discussions, patient mental health, medical care near death, and caregiver bereavement adjustment. *JAMA*. 2008;300(14):1665-1673. doi:10.1001/jama.300.14.1665
38. Julious SA. Sample sizes for clinical trials with normal data. *Stat Med*. 2004;23(12):1921-1986. doi:10.1002/sim.1783
39. Piaggio G, Elbourne DR, Pocock SJ, et al. Reporting of noninferiority and equivalence randomized trials: extension of the CONSORT 2010 statement. *JAMA*. 2012;308(24):2594-2604. doi:10.1001/jama.2012.87802
40. Kurland BF, Johnson LL, Egleston BL, Diehr PH. Longitudinal data with follow-up truncated by death: match the analysis method to research aims. *Stat Sci*. 2009;24(2):211. doi:10.1214/09-STS293
41. Colantuoni E, Scharfstein DO, Wang C, et al. Statistical methods to compare functional outcomes in randomized controlled trials with high mortality. *BMJ*. 2018;360:j5748. doi:10.1136/bmj.j5748
42. Bender CM, Ergün FS, Rosenzweig MQ, et al. Symptom clusters in breast cancer across 3 phases of the disease. *Cancer Nurs*. 2005;28(3):219-225. doi:10.1097/00002820-200505000-00011
43. Glickman ME, Rao SR, Schultz MR. False discovery rate control is a recommended alternative to Bonferroni-type adjustments in health studies. *J Clin Epidemiol*. 2014;67(8):850-857. doi:10.1016/j.jclinepi.2014.03.012
44. Earle CC, Park ER, Lai B, et al. Identifying potential indicators of the quality of end-of-life cancer care from administrative data. *J Clin Oncol*. 2003;21(6):1133-1138. doi:10.1200/JCO.2003.03.0509
45. Earle CC, Landrum MB, Souza JM, et al. Aggressiveness of cancer care near the end of life: is it a quality-of-care issue? *J Clin Oncol*. 2008;26(23):3860-3866. doi:10.1200/JCO.2007.15.8253
46. McCarthy EP, Burns RB, Ngo-Metzger Q, et al. Hospice use among Medicare managed care and fee-for-service patients dying with cancer. *JAMA*. 2003;289(17):2238-2245. doi:10.1001/jama.289.17.2238
47. Yoong J, Park ER, Greer JA, et al. Early palliative care in advanced lung cancer: a qualitative study. *JAMA Intern Med*. 2013;173(4):283-290. doi:10.1001/jamainternmed.2013.1874
48. Zimmermann C, Mathews J. Palliative care is the umbrella, not the rain—a metaphor to guide conversations in advanced cancer. *JAMA Oncol*. 2022;8(5):681-682. doi:10.1001/jamaoncol.2021.8210
49. Sedhom R, Shulman LN, Parikh RB. Precision palliative care as a pragmatic solution for a care delivery problem. *J Clin Oncol*. 2023;41(16):2888-2892. doi:10.1200/JCO.22.02532
50. Temel JS, Shaw AT, Greer JA. Challenge of prognostic uncertainty in the modern era of cancer therapeutics. *J Clin Oncol*. 2016;34(30):3605-3608. doi:10.1200/JCO.2016.67.8573
51. Zimmermann C, Pope A, Hannon B, et al. Phase II trial of symptom screening with targeted early palliative care for patients with advanced cancer. *J Natl Compr Canc Netw*. 2021;20(4):361-370.e3. doi:10.6004/jnccn.2020.7803
52. Zimmermann C, Pope A, Hannon B, et al. Symptom screening with targeted early palliative care (STEP) versus usual care for patients with advanced cancer: a mixed methods study. *Support Care Cancer*. 2023;31(7):404. doi:10.1007/s00520-023-07870-9
53. Greer JA, Pirl WF, Jackson VA, et al. Effect of early palliative care on chemotherapy use and end-of-life care in patients with metastatic non-small-cell lung cancer. *J Clin Oncol*. 2012;30(4):394-400. doi:10.1200/JCO.2011.35.7996
54. Dy SM, Kiley KB, Ast K, et al. Measuring what matters: top-ranked quality indicators for hospice and palliative care from the American Academy of Hospice and Palliative Medicine and Hospice and Palliative Nurses Association. *J Pain Symptom Manage*. 2015;49(4):773-781. doi:10.1016/j.jpainsymman.2015.01.012
55. He JC, Moffat GT, Podolsky S, et al. Machine learning to allocate palliative care consultations during cancer treatment. *J Clin Oncol*. 2024;42(14):1625-1634. doi:10.1200/JCO.23.01291
56. Maringe C, Spicer J, Morris M, et al. The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in England, UK: a national, population-based, modelling study. *Lancet Oncol*. 2020;21(8):1023-1034. doi:10.1016/S1473-0750(20)30388-0
57. Bhalla S, Bakouny Z, Schmidt AL, et al. Care disruptions among patients with lung cancer: a COVID-19 and cancer outcomes study. *Lung Cancer*. 2021;160:78-83. doi:10.1016/j.lungcan.2021.07.002