Effects of a Palliative Care Intervention on Clinical Outcomes in Patients With Advanced Cancer
The Project ENABLE II Randomized Controlled Trial

Marie Bakitas, DNSc, APRN
Kathleen Doyle Lyons, ScD, OTR
Mark T. Hegel, PhD
Stefan Balan, MD
Frances C. Brokaw, MD, MS
Janette Seville, PhD
Jay G. Hull, PhD
Zhongze Li, MS
Tor D. Tosteson, ScD
Ira R. Byock, MD
Tim A. Ahles, PhD

IFTY PERCENT OF PERSONS WITH cancer are not cured of their disease; however, with improved treatment even patients with advanced disease may live for years. Providing palliative care concurrent with oncology treatment has been proposed to improve quality of life for patients with advanced cancer. The National Consensus Project Clinical Practice Guidelines for Quality Palliative Care recommends palliative care referral at the time of a life-threatening diagnosis and other core elements including a multidimensional assessment to identify, prevent, and alleviate suffering; interdisciplinary team evaluation and treatment in selected cases; effective communication skills and assistance with medical decision making; skill in the care of those dying and bereaved; continuity of care; equitable access; and commitment to continued improvement and excellence.

Context There are few randomized controlled trials on the effectiveness of palliative care interventions to improve the care of patients with advanced cancer.

Objective To determine the effect of a nursing-led intervention on quality of life, symptom intensity, mood, and resource use in patients with advanced cancer.

Design, Setting, and Participants Randomized controlled trial conducted from November 2003 through May 2008 of 322 participants with advanced cancer in a rural, National Cancer Institute–designated comprehensive cancer center in New Hampshire and affiliated outreach clinics and a VA medical center in Vermont.

Interventions A multicomponent, psychoeducational intervention (Project ENABLE [Educate, Nurture, Advise, Before Life Ends]) conducted by advanced practice nurses consisting of 4 weekly educational sessions and monthly follow-up sessions until death or study completion (n = 161) vs usual care (n = 161).

Main Outcome Measures Quality of life was measured by the Functional Assessment of Chronic Illness Therapy for Palliative Care (score range, 0-184). Symptom intensity was measured by the Edmonton Symptom Assessment Scale (score range, 0-900). Mood was measured by the Center for Epidemiological Studies Depression Scale (range, 0-60). These measures were assessed at baseline, 1 month, and every 3 months until death or study completion. Intensity of service was measured as the number of days in the hospital and in the intensive care unit (ICU) and the number of emergency department visits recorded in the electronic medical record.

Results A total of 322 participants with cancer of the gastrointestinal tract (41%; 67 in the usual care group vs 66 in the intervention group), lung (36%; 58 vs 59), genitourinary tract (12%; 20 vs 19), and breast (10%; 16 vs 17) were randomized. The estimated treatment effects (intervention minus usual care) for all participants were a mean (SE) of 4.6 (2) for quality of life (P = .02), −27.8 (15) for symptom intensity (P = .06), and −1.8 (0.81) for depressed mood (P = .02). The estimated treatment effects in participants who died during the study were a mean (SE) of 8.6 (3.6) for quality of life (P = .02), −24.2 (20.5) for symptom intensity (P = .24), and −2.7 (1.2) for depressed mood (P = .03). Intensity of service did not differ between the 2 groups.

Conclusion Compared with participants receiving usual oncology care, those receiving a nurse-led, palliative care–focused intervention addressing physical, psychological, and social care coordination provided concurrently with oncology care had higher scores for quality of life and mood, but did not have improvements in symptom intensity scores or reduced days in the hospital or ICU or emergency department visits.

Trial Registration clinicaltrials.gov Identifier: NCT00253383
PALLIATIVE CARE INTERVENTION FOR PATIENTS WITH ADVANCED CANCER

RESULTS is not included in this article.

grief), but a discussion of those re-
cognition (ER−), human epidermal
or liver metastasis, estrogen receptor
or IV non–small cell or extensive small
cell), genitourinary tract (stage IV), or
breast (stage IV and visceral crisis, lung
or liver metastasis, estrogen receptor
negative [ER−], human epidermal
growth factor receptor 2 positive [Her
2 neu+] cancer. Patients with im-
paired cognition (<17 on a modified
Mini-Mental State Examination), an
Axis I psychiatric disorder (schizophrenia,
bipolar disorder), or active substance
use were excluded. Patients were
asked to select a caregiver to partici-
pate in the study. Patients who did not
select a caregiver were not excluded.

Methods
Study Design
The study was a randomized controlled
trial of a palliative care intervention com-
pared with usual care for persons newly
diagnosed with advanced cancer. The
primary end points were patient-
reported quality of life, symptom inten-
sity, and resource use. Mood was a sec-
tary outcome. Enrollment began in
Data collection of patient-reported out-
comes ended on December 31, 2007.
However, outcomes that could be moni-
tored via chart review (eg, resource use
and vital status) were collected through
May 1, 2008. The study protocol and data
and safety monitoring board plan were
approved by the institutional review
boards of the Norris Cotton Cancer
Center and Dartmouth College in Lebanon,
New Hampshire, and the Veterans Ad-
ministration (VA) medical center in
White River Junction, Vermont. All pa-
tient and caregiver participants signed a
document confirming their informed
consent.

Patients
Patients identified at the Norris Cot-
ton Cancer Center’s tumor boards with a
life-limiting cancer (prognosis of ap-
proximately 1 year) were eligible if they
were within 8 to 12 weeks of a new di-
nosis of gastrointestinal tract (unre-
sectable stage III or IV), lung (stage IIIB
or IV non–small cell or extensive small
cell), genitourinary tract (stage IV), or
breast (stage IV and visceral crisis, lung
or liver metastasis, estrogen receptor
negative [ER−], human epidermal
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pate in the study. Patients who did not
select a caregiver were not excluded.

Patients and their caregiver were ran-
donically assigned to the intervention or
usual care using a stratified random-
ization scheme developed for each of
the 2 primary sites (Norris Cotton Can-
ter, VA Medical Center). The schemes were stratified by disease and
blocked within strata (block lengths of
2 and 4 varied randomly). Research as-
sistants notified the participant of group
allocation when the baseline assess-
ment was returned. Referring clini-
cians were neither informed nor for-
mally blinded to participant assignment.

Intervention
The intervention has been described in
detail elsewhere. Briefly, the interven-
tion, based on the chronic care model,
used a case management, educational ap-
proach to encourage patient activation,
self-management, and empowerment.
We refined and converted the in-
person and group strategies used in our
prior studies and demonstration project
to a manualized, telephone-
based format to improve access to pal-
liative care in a rural population. One of
2 advanced practice nurses with pallia-
tive care specialty training conducted 4
initial structured educational and prob-
lem-solving sessions and at least monthly
telephone follow-up sessions until the
participant died or the study ended. Ad-
vanced practice nurses’ caseloads were
balanced by diagnosis and sex.

The advanced practice nurses began
all contacts with an overall assessment
by administering the Distress Thermom-
eter, an 11-point rating scale (0-10) of
distress recommended by the National
Comprehensive Cancer Network guide-
lines. In addition to an overall inten-
sity rating, the Distress Thermometer
identified sources of distress in the 5 areas
of practical problems (eg, work or
school), family problems, emotional
problems, spiritual or religious con-
cerns, and physical problems. If dis-
tress intensity was rated greater than 3,
the advanced practice nurses explored
the sources of distress and identified if
the participant would like to apply the
problem-solving approach to address his
or her issues. The nurse then covered the
assigned module for that session. The
education manual entitled “Charting Your
Course: An Intervention for People and
Families Living With Cancer,” devel-
oped during ENABLE I, contained the
4 modules of problem solving,
communication and social support,
symptom management, advance care
planning and unfinished business, and
an appendix listing supportive care
resources (available from the authors
or at http://www.cancer.dartmouth.
edu/palliative/index.shtml).

On average, session 1 (introduction
and problem solving) lasted 41 min-
utes and sessions 2 through 4 each lasted
30 minutes. Following the 4 formal ses-
sions, the advanced practice nurse was
readily available by telephone and also
contacted the participant (or care-
giver) at least monthly (until the par-
ticipant’s death) to follow up on active
issues and to assess the need for refer-
ral to appropriate care resources (eg, pal-
liative care team, hospice). When con-
cerns were identified, participants were
encouraged to contact the oncology or
palliative care clinical teams (if they had
received a palliative care team consultation). However, with the participant’s permission, the advanced practice nurses would contact the appropriate clinical team about issues requiring attention (eg, unrelied pain) or referrals to community resources (eg, spiritual counselor).

The clinical teams were responsible for all medical decisions including medication and inpatient care management; however, the advanced practice nurses, in consultation with the team, could facilitate referrals to ancillary resources. Additionally, intervention participants and their caregiver were invited to attend monthly group shared medical appointments (SMAs)27,28 led by a certified palliative care physician and nurse practitioner. These appointments allowed participants and caregivers to ask questions about medical problems or related issues (eg, symptom management, insurance, social services) and to have more in-depth discussions than is practical during typical clinic visits.28

Training of study interventionists in problem solving and group medical appointments was provided by one of the study team psychologists (J.S.). Initial training took approximately 20 hours for the 2 nurse interventionists and 12 hours for the nurse practitioner and physician SMA facilitators. Training methods included didactic presentations, written treatment manuals, and role-playing with feedback (all training materials are available on request from the authors). Thereafter, the study team, including the palliative care–certified nurse practitioner and physician, psychologists, and other team members, met bimonthly to review advanced practice nurses’ audio-taped educational sessions and to provide feedback on difficult patient management issues.

Usual Care

Participants assigned to usual care were allowed to use all oncology and supportive services without restrictions including referral to the institutions’ interdisciplinary palliative care service. The VA Medical Center site had an advanced illness coordinated care program that provided consultation to oncology staff for inpatients with life-limiting illness.

Data Collection and Instruments

Participants completed baseline questionnaires upon enrollment. Follow-up questionnaires were mailed 1 month after baseline and every 3 months until the participant died or study completion (December 31, 2007). Quality of life was measured by the Functional Assessment of Chronic Illness Therapy for Palliative Care.29,30 This 46-item tool measures physical, emotional, social, and functional well-being in addition to concerns relevant to persons with life-threatening illness (eg, feeling peaceful, reconciling with others). Scores for this tool range from 0 to 184, and higher scores indicate better quality of life (Cronbach α = .80 for our sample). Symptom intensity was measured by a modified Edmonton Symptom Assessment Scale (ESAS).31,32 The ESAS assessed the 9 symptoms of pain, activity, nausea, depression, anxiety, drowsiness, appetite, sense of well-being, and shortness of breath, using numerical visual analog scales with discrete check boxes (range, 0-10). Scores were multiplied by 10 to allow comparisons with other studies that used a 100-cm line to calculate symptom intensity. The scores in this study range from 0 to 900, which are consistent with other studies, and higher scores indicate greater symptom intensity (Cronbach α = .80 for our sample). Mood was measured by the Center for Epidemiological Studies Depression Scale (CES-D), an established 20-item measure33,34 with scores from 0 to 60. A score of 16 or higher generally indicates a clinically significant level of depressed mood35 (Cronbach α = .84 for our sample). Data on resource use (number of days in the hospital, number of days in the intensive care unit [ICU], and number of emergency department visits) and vital status were collected by chart review until death or May 1, 2008. Patients completed a self-report demographic questionnaire including age, sex, ethnicity (Hispanic or Latino), race (white, American Indian/Native Alaskan, Asian, Native Hawaiian/other Pacific Islander, black/African American, or other), religious affiliation, marital status, other members of household, employment status, occupation, and level of education.

Statistical Analysis

The original target sample size of 400 was chosen to provide 80% power to detect treatment effects of at least 0.33 SDs for scores on the Functional Assessment of Chronic Illness Therapy for Palliative Care, ESAS, and CES-D based on a t test comparing the treatment groups with respect to the last observed value with a 2-sided α of .01. However, at the planned study completion date, the final total study enrollment was 322 due to slightly slower accrual than anticipated.

Our primary outcome measures were quality of life (assessed with the Functional Assessment of Chronic Illness Therapy for Palliative Care), symptom intensity (assessed with the ESAS), and resource use. Mood (assessed with the CES-D) was a secondary outcome. For quality of life, symptom intensity, and mood, we conducted 2 sets of longitudinal, intention-to-treat analyses for all participants with baseline and 1 or more follow-up assessments using repeated measures analysis of covariance to examine the effect of the intervention on (1) the total sample in the year after enrollment and (2) the sample of participants who died.

In the first set of analyses, we proceeded forward in time from enrollment. Baseline outcome data were used as adjusting variables. Adjusted means were estimated for the intention-to-treat groups and included all assessment data. For these analyses, we applied a mixed-effects model for repeated measures to the longitudinal data using random-subject effects to account for correlation between repeated outcome measurements on the same individual. Confidence intervals (CIs) and P values were formed for the overall average effects.

The second set of analyses was restricted to the sample of participants who died during the study (as of the final chart
review on May 1, 2008) and had completed both baseline and 1 or more additional assessments. We applied the same intention-to-treat longitudinal model to estimate the mean overall treatment effect for this subsample using the 3 assessments prior to death.

Mean, median, and maximum values were calculated for chart review data on number of days in the hospital, number of days in the ICU, and number of emergency department visits at baseline and the sums of the total days and visits over the length of enrollment. Groups were compared using the Wilcoxon rank sum test.

We examined the baseline covariates that were predictive of missing data and found that both treatment and the baseline outcomes were statistically significant predictors. We then included these as adjusting variables in the analyses to meet the conditions for missing at random.35 Two-sided $P<.05$ was set as statistically significant. All calculations were performed using SAS software version 9.1 (SAS Institute, Cary, North Carolina).

We did an exploratory, post hoc analysis of survival. We used a log-rank test to compare Kaplan-Meier survival curves for the 2 groups.

**RESULTS**

Of 1222 patients screened between November 2003 and May 2007, 681 were eligible and were approached and 322 were enrolled (47% participation rate) (Figure 1). Following consent, participants were randomly assigned to receive usual care ($n=161$) or the intervention ($n=161$). Subsequently, 27 individuals assigned to usual care and 16 individuals assigned to the intervention dropped out (Figure 1). A total of 134 participants in the usual care group and 145 participants in the intervention group were analyzed for patient-reported outcomes.

The Table shows no statistically significant differences at baseline between the intervention and usual care groups for demographic and clinical characteristics, the use of chemotherapy or radiation anticancer treatments, advance directives, palliative care or hospice referral, number of days in the hospital or ICU, or number of emergency department visits. Our sample included slightly more men than is typical of the general population due to the predominant male population at the VA Medical Center recruitment site. During the course of the study, there was no statistically significant difference between the groups relative to the number of participants who received parenteral chemotherapy (72% [116/161] in the usual care group vs 74% [119/161] in the intervention group; Fisher exact test, $P=.80$) or radiation therapy (21% [34/161] in the usual care group vs 22% [36/161] in the intervention group; Fisher exact test $P=.89$).

Of the 681 eligible patients, there were no statistically significant differences between participants ($n=322$) and non-participants ($n=359$) relative to age, sex, Karnofsky Performance Scale score, receipt of chemotherapy or radiation therapy, performance status, emergency department visits, advance directives, palliative care or hospice referral, or number of days in the ICU in the prior 3 months.

**Quality of Life, Symptom Intensity, and Mood**

There were no statistically significant differences at baseline between the groups for the 3 patient-reported outcomes (Table). Longitudinal intention-to-treat analyses for the total sample revealed higher quality of life (mean [SE], 4.6 [2]; $P=.02$) (Functional Assessment of Chronic Illness Therapy for Palliative Care).
<table>
<thead>
<tr>
<th>Demographic Characteristics</th>
<th>Survival Outcomes Sample</th>
<th>Patient Outcomes Sample</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intervention (n = 161)</td>
<td>Usual Care (n = 161)</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>64.7 (10.8)</td>
<td>65.4 (11.6)</td>
</tr>
<tr>
<td>Male sex</td>
<td>96 (59.6)</td>
<td>91 (56.5)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never married</td>
<td>12 (7.4)</td>
<td>15 (9.3)</td>
</tr>
<tr>
<td>Married or living with partner</td>
<td>116 (72.1)</td>
<td>105 (65.2)</td>
</tr>
<tr>
<td>Divorced or separated</td>
<td>19 (11.8)</td>
<td>23 (14.3)</td>
</tr>
<tr>
<td>Widowed</td>
<td>14 (8.7)</td>
<td>13 (11.2)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;High school graduate</td>
<td>17 (10.5)</td>
<td>20 (12.4)</td>
</tr>
<tr>
<td>High school graduate</td>
<td>83 (51.5)</td>
<td>74 (46.0)</td>
</tr>
<tr>
<td>College graduate</td>
<td>43 (26.7)</td>
<td>38 (23.6)</td>
</tr>
<tr>
<td>Missing</td>
<td>18 (11.3)</td>
<td>29 (16.0)</td>
</tr>
<tr>
<td>Race&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>143 (89.0)</td>
<td>132 (82.0)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (1.2)</td>
<td>2 (1.2)</td>
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<tr>
<td>Missing</td>
<td>16 (9.9)</td>
<td>27 (16.8)</td>
</tr>
<tr>
<td>Religion</td>
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<td></td>
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<tr>
<td>Protestant</td>
<td>68 (42.2)</td>
<td>60 (37.3)</td>
</tr>
<tr>
<td>Catholic</td>
<td>44 (27.3)</td>
<td>42 (26.1)</td>
</tr>
<tr>
<td>Jewish</td>
<td>3 (1.9)</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Other</td>
<td>25 (15.5)</td>
<td>29 (18.0)</td>
</tr>
<tr>
<td>Missing</td>
<td>21 (13.0)</td>
<td>29 (18.0)</td>
</tr>
<tr>
<td>Work status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>33 (20.5)</td>
<td>30 (18.6)</td>
</tr>
<tr>
<td>Retired</td>
<td>80 (49.7)</td>
<td>82 (50.9)</td>
</tr>
<tr>
<td>Not employed</td>
<td>45 (27.9)</td>
<td>48 (30.0)</td>
</tr>
<tr>
<td>Missing</td>
<td>3 (1.9)</td>
<td>1 (0.6)</td>
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<tr>
<td>VA medical center enrollment site</td>
<td>43 (26.7)</td>
<td>41 (25.5)</td>
</tr>
<tr>
<td>Lives in rural area</td>
<td>86 (53.4)</td>
<td>95 (59.0)</td>
</tr>
<tr>
<td>Caregiver enrolled</td>
<td>116 (72)</td>
<td>104 (64.6)</td>
</tr>
<tr>
<td>Primary disease site</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal tract</td>
<td>66 (41.0)</td>
<td>67 (41.6)</td>
</tr>
<tr>
<td>Lung</td>
<td>59 (36.6)</td>
<td>58 (36.0)</td>
</tr>
<tr>
<td>Genitourinary tract</td>
<td>19 (11.8)</td>
<td>20 (12.4)</td>
</tr>
<tr>
<td>Breast</td>
<td>17 (10.6)</td>
<td>16 (9.9)</td>
</tr>
<tr>
<td>Anticancer treatment at enrolment</td>
<td>137 (85.1)</td>
<td>134 (83.2)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>20 (12.4)</td>
<td>21 (13.0)</td>
</tr>
<tr>
<td>Radiation therapy</td>
<td>77.9 (11.1)</td>
<td>76.6 (13.1)</td>
</tr>
<tr>
<td>Karnofsky Performance Status, mean (SD)&lt;sup&gt;e,f&lt;/sup&gt;</td>
<td>134.0 (22.8)</td>
<td>129.7 (26.2)</td>
</tr>
<tr>
<td>Test score, mean (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Functional Assessment of Chronic Illness Therapy for Palliative Care (n = 273)</td>
<td>282.5 (148.8)</td>
<td>286.3 (154.0)</td>
</tr>
<tr>
<td>Center for Epidemiological Studies Depression Scale (n = 268)</td>
<td>12.1 (8.5)</td>
<td>13.8 (8.9)</td>
</tr>
<tr>
<td>Type of advance directive&lt;sup&gt;g&lt;/sup&gt;</td>
<td>69 (42.9)</td>
<td>76 (47.2)</td>
</tr>
<tr>
<td>Living will</td>
<td>68 (42.2)</td>
<td>78 (48.4)</td>
</tr>
<tr>
<td>Durable power of attorney for health care</td>
<td>13 (8.1)</td>
<td>10 (6.2)</td>
</tr>
<tr>
<td>Do not resuscitate order</td>
<td>2 (1.2)</td>
<td>2 (1.2)</td>
</tr>
<tr>
<td>Referral to hospice&lt;sup&gt;h&lt;/sup&gt;</td>
<td>42 (26.1)</td>
<td>51 (31.7)</td>
</tr>
<tr>
<td>Referral to palliative care&lt;sup&gt;h&lt;/sup&gt;</td>
<td>2.8 (0) [25]</td>
<td>3.1 (0) [25]</td>
</tr>
<tr>
<td>Resource use in prior 3 mo, mean (median) [maximum]&lt;sup&gt;i&lt;/sup&gt;</td>
<td>0.02 (0) [2]</td>
<td>0.04 (0) [2]</td>
</tr>
</tbody>
</table>

<sup>a</sup>Values are expressed as number (percentage) unless otherwise indicated. Percentages may not equal 100% due to rounding.
<sup>b</sup>The Fisher exact test was used for categorical variables and the t test was used for continuous variables.
<sup>c</sup>No participants were of Hispanic ethnicity or black race.
<sup>d</sup>For the survival outcomes sample, the total number of patients is 273; for the patient outcomes sample, the total number of patients is 279.
<sup>e</sup>Based on chart review.
<sup>f</sup>Values calculated using the Wilcoxon rank sum test.

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Care scores in Figure 2), a trend toward lower symptom intensity (mean [SE], −27.8 [15]; P = .06) (ESAS scores in Figure 2), and lower depressed mood (mean [SE], −1.8 [0.81]; P = .02) (CES-D scores in Figure 2) in the intervention group compared with the usual care group.

Longitudinal analyses for the subset of participants who died during the study revealed a similar pattern of effects for higher quality of life (mean [SE], 8.6 [3.6]; P = .02) (Functional Assessment of Chronic Illness Therapy for Palliative Care scores in Figure 3) and no differences in symptom intensity (mean [SE], −24.2 [20.5]; P = .24) (ESAS scores in Figure 3) and lower depressed mood (mean [SE], −2.7 [1.23]; P = .03) (CES-D scores in Figure 3) in the intervention group compared with the usual care group.

Resource Use

There were no statistically significant differences between groups in the number of days in the hospital (6.6 vs 6.5, respectively; P = .14), number of days in the ICU (0.06 vs 0.06; P = .99), or in the number of emergency department visits (0.86 vs 0.63; P = .53) (as of the final chart review on May 1, 2008).
the usual care group were alive at the final chart review (May 1, 2008) and were censored.

**COMMENT**

This study shows that integration of a nurse-led palliative care intervention concurrent with anticancer treatments demonstrated higher quality of life (measured by an instrument designed for this specific population), lower depressed mood, but limited effect on symptom intensity scores and use of resources in intervention participants relative to those receiving usual cancer care. The intervention had no effect on the number of days in the hospital and ICU, the number of emergency department visits, or anticancer treatment because the proportions of participants in each group receiving these therapies were similar. To our knowledge, this is the first randomized controlled trial designed to test a palliative care intervention concurrent with oncology treatment as has been recommended by international guidelines and consensus recommendations.

A systematic review of specialized palliative care identified 22 trials (16 from the United States) between 1984-2007 with a median sample size of 204, half exclusively with cancer patients. It suggested that evidence for the effectiveness of this care was sparse and limited by methodological shortcomings including control group contamination, recruitment, attrition, and adherence issues. Our trial addressed these issues and contributes to the increasing evidence that palliative care may improve quality of life and mood at the end of life, which are 2 of the main targets of care. In our study, intervention participants’ higher quality of life and lower depressed mood may be attributed to improved psychosocial and emotional well-being. Mood is a determinant of the experience of quality of life and suffering despite a mounting burden of physical symptoms. However, while patients in the intervention group had improved in these outcomes, we conservatively planned our original target enrollment of 400 based on a significance level of .01. Statistical inferences based on this stringent critical value would lead to the conclusion that there were no statistically significant differences between groups in quality of life or mood.

There is no universally accepted definition of the magnitude of difference in quality-of-life scores that is considered clinically meaningful or clinically important. Differences between groups of 4% for improvement or 9% for worsening have been cited as clinically meaningful differences using the Functional Assessment of Cancer Therapy tool and we found such between-group differences in our scores. Others have recommended using a distribution-based approach to compare 2 subgroups relative to the SD or SE. Differences between 0.5 and 1 SD or 1 SE are considered statistically significant for most health-related quality-of-life instruments. In our study, the quality of life and mood scores demonstrated a greater than 1 SE difference between groups. By these benchmarks, group differences for quality of life and mood achieved clinical significance in addition to statistical significance.

The results did not demonstrate a group difference in symptom intensity as measured by the ESAS. In a systematic review of palliative care effectiveness, which included 14 studies that measured symptom intensity using a variety of scales, only 1 demonstrated improvement of 1 of the targeted symptoms (dyspnea). In that study, the palliative care physician contacted the patients’ primary care physician directly with symptom management recommendations. It is possible that an intervention focused primarily on patient empowerment is not robust enough to achieve improved symptom management. Alternatively, the mean ESAS scores (scale range, 0-900) were essentially in the 200s (equivalent to a rating of 2 on a scale of 0 to 10) for both groups. There may be little room for improvement because usual care participants also reported relatively low symptom intensity scores compared with patients with advanced cancer in other studies. It may be unrealistic to expect to reduce symptoms further in the setting of progressive disease. Finally, it is possible that symptoms were intermittently improved but the ESAS tool or our data collection schedule may not have been sensitive enough to accurately portray the dynamic, multidimensional symptom experience of this sample. It is not clear which, if any, of these reasons explain why the intervention group had improved quality of life without symptom improvement. However, quality of life and mood are still high-priority patient-centered goals.

The intervention was designed to educate and provide ongoing support to patients (from diagnosis to death) with life-limiting cancers and their caregivers about symptom management, advance care planning, treatment decision making, and communication. Beyond education, we hoped to activate patients by coaching them to enhance their coping and problem-solving skills over the illness trajectory. The intervention emphasized the importance of patients taking an active role in openly communicating with family and the oncology team regarding their values, priorities, and treatment preferences.
There was particular emphasis on communicating during times when anticancer treatments were less likely to halt disease progression or alleviate symptoms.68 Such communication has recently been demonstrated to be associated with improved quality of life, reduced use of aggressive treatments at the end of life, and increased length of hospice stays.69 Unlike other studies that were specifically designed to evaluate costs,50,51 our intervention did not demonstrate reduced use of hospital, ICU, or emergency department resources compared with usual care. However, data collection via chart review may have missed participants’ use of resources. Use of databases that may more comprehensively capture costs (eg, Medicare) would address such limitations.52,53

Oncology palliative care may lead to positive outcomes by a number of mechanisms. First, interventions may lead to increased social support,54 patient activation (self-advocacy), or more coordinated and improved medical care. These factors may in turn lead to improved clinical outcomes.22,23,47 Second, meta-analyses in the United States53 and Europe56 of more than 10,000 cancer patients in clinical trials that measured quality of life demonstrated a strong association between higher quality of life and longer survival. Third, palliative and hospice care have been associated with less aggressive cancer care, such as reduced use of chemotherapy in the days before death and reduced inappropriate use of hospital and ICU resources in terminal patients—factors that may influence patients’ quality of life.51 Finally, Nelson et al28 proposed a biobehavioral model whereby interventions that enhance quality of life may positively influence the psychoneuroimmunologic axis and improve physiological clinical outcomes. Identifying mechanisms of intervention effect on quality of life is an important future area of research.

A number of limitations are worthy of note. First, consistent with the pacity of racial and ethnic diversity in this rural New England region from which our sample was drawn, we had limited ethnic and racial representation and therefore recognize the need to replicate this study with more diverse populations. Second, our intervention was primarily conducted by telephone, a strategy that has shown promise in the delivery of psychotherapy59 and in encouraging screening behaviors.60 It is possible that a more robust effect, particularly in reducing symptom intensity, may have been seen with in-person interactions (such as those seen in another successful outpatient palliative care intervention study61) rather than our telephone-based approach. However, in-person consultation was often not feasible for our debilitated, rural population, many of whom live more than an hour’s drive from the cancer center. Further research is needed to explore optimal care delivery systems in this population.

Institute of Medicine reports,2,3 the National Consensus Project for Quality Palliative Care,9 other consensus panels,62,63 and oncology professional societies39 agree that comprehensive cancer care must incorporate more than state-of-the-art disease-modifying treatment. Comprehensive, high-quality cancer care includes interdisciplinary attention to improving physical, psychological, social, spiritual, and existential concerns for the patient and his or her family. While our study did not show that early intervention for patients with advanced cancer by a nurse-led program improved symptoms or reduced use of some resources, the study did show that it provides some patients with advanced cancer a higher quality of life and mood.

Author Affiliations: Departments of Anesthesiology, Section of Palliative Medicine (Dr Bakitas, Brokaw, and Byock), Psychiatry (Dr Lyons, Hegel, Seville, and Ahles), and Medicine (Dr Balan and Brokaw), Dartmouth Medical School, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire; Department of Psychological and Brain Sciences, Dartmouth College, Hanover, New Hampshire (Dr Hull); School of Nursing, Yale University, New Haven, Connecticut (Dr Bakitas); White River Junction VA Medical Center, White River Junction, Vermont (Dr Balan); Biotistics Shared Resource, Norris Cotton Cancer Center, Lebanon, New Hampshire (Mr Li and Dr Tosteson); and Department of Psychiatry, Memorial Sloan-Kettering Cancer Center, New York, New York (Dr Ahles).

Author Contributions: Dr Bakitas had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Bakitas, Seville, Ahles. Acquisition of data: Bakitas, Lyons, Hegel, Balan, Brokaw, Ahles. Analysis and interpretation of data: Bakitas, Lyons, Hegel, Balan, Brokaw, Hull, Li, Tosteson, Byock, Ahles. Drafting of the manuscript: Bakitas, Lyons, Hegel, Brokaw, Hull, Tosteson, Ahles. Critical revision of the manuscript for important intellectual content: Bakitas, Lyons, Hegel, Balan, Brokaw, Seville, Hull, Li, Tosteson, Byock, Ahles. Statistical analysis: Bakitas, Hull, Li, Tosteson. Obtained funding: Bakitas, Ahles. Administrative, technical, or material support: Bakitas, Lyons, Hegel, Balan, Brokaw, Li, Tosteson, Byock.

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PALLIATIVE CARE INTERVENTION FOR PATIENTS WITH ADVANCED CANCER

National Consensus Project for Quality Palliative Care; 2004.


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