Original Article

Extent and Determinants of Terminally Ill Cancer Patients' Concordance Between Preferred and Received Life-Sustaining Treatment States: An Advance Care Planning Randomized Trial in Taiwan

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Abstract
Context. Promoting patient value-concordant end-of-life care is a priority in health care systems but has rarely been examined in randomized clinical trials.

Objectives. To examine the effectiveness of an advance care planning intervention in facilitating concordance between cancer patients' preferred and received life-sustaining treatment (LST) states and to explore modifiable factors facilitating or impeding such concordance.

Methods. Terminal cancer patients ($N = 460$) were randomly assigned 1:1 to the experimental and control arms of a randomized clinical trial, with 430 deceased participants comprising the final sample. States of preferred LSTs (cardiopulmonary resuscitation, intensive care unit care, chest compression, intubation with mechanical ventilation, intravenous nutrition, and nasogastric tube feeding) and LSTs received in the last month were examined by hidden Markov modeling. Concordance and its modifiable predictors were evaluated by kappa and multivariate logistic regression, respectively.

Results. We identified three LST-preference states (uniformly preferring LSTs, rejecting LSTs except intravenous nutrition support, and mixed LST preferences) and three received LST states (uniformly receiving LSTs, received intravenous nutrition only, and selectively receiving LSTs). Concordance was not significantly higher in the experimental than the control arm (kappa [95% CI]: 0.126 [0.032, 0.221] vs. 0.050 [−0.028, 0.128]; arm difference: odds ratio [95% CI]: 1.008 [0.675, 1.5001]). Preferred-received LST-state concordance was facilitated by accurate prognostic awareness, better quality of life, and more depressive symptoms, whereas concordance was impeded by more anxiety symptoms.

Conclusions. Our advance care planning intervention did not facilitate concordance between terminally ill cancer patients' preferred and received LST states, but patient value-concordant end-of-life care may be facilitated by interventions to cultivate accurate prognostic awareness, improve quality of life, support depressive patients, and clarify anxious patients' overexpectations of LST efficacy.   J Pain Symptom Manage 2019;58:1−10. © 2019 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.

Key Words
Value concordance, psychological symptoms, quality of life, randomized controlled trial, end-of-life care

Introduction

Promoting patient value-concordant end-of-life (EOL) care is a priority in health care systems[1,2] to counteract increasingly intensive and costly EOL-cancer care,[3–5] which is often more aggressive than patients prefer,[6] leading to not only patients' wishes being not honored but also poor EOL-care quality.[7,8] However, effectiveness in promoting value-concordant EOL care has rarely been examined in randomized clinical trials (RCTs) to improve advanced care planning (ACP).[9–12]

Among these RCTs, none targeted cancer patients for whom individualized EOL care is extremely pertinent.[13,14] Furthermore, these RCTs' rigor, hence the robustness of their positive findings[10,11] on facilitating value-concordant EOL care, is threatened by some methodological issues.[14,15] All studies,[9–12] except one,[9] provided a single-session intervention long before the patient's death, as shown by long mean postenrollment survivals (362.2–388.8 days)[10] or few (13.67%[11]–18.12%)[9] patients dying within 6 months of enrollment when concordance between preferred and received EOL care was evaluated. These concordance studies commonly fail to directly assess patients' EOL-care preferences[9,10,12] and do not evaluate EOL-care preferences more than once[9–11] to capture their dynamic changes over time,[16] possibly distorting the extent to which patients' EOL-care preferences are honored. These studies did not explicitly indicate how treatment fidelity was ensured.[9–11]

Most importantly, these studies commonly evaluated preferred "goals of EOL care,"[9,10,12] which frequently differ from preferences for specific life-sustaining treatments (LSTs)[17] that patients must decide to receive or decline at EOL. However, assessing preferences for multiple LSTs[11] in busy clinical settings may be complicated and impractical. Parsimoniously identifying LST-preference states (sets of LST preferences ["latent states"] rather than preferences for individual LSTs) minimizes the time clinicians spend assessing LST preferences and avoids burdening terminally ill patients with choosing among multiple individual LSTs. Furthermore, because ACP studies have provided limited evidence for improving EOL-care quality by honoring terminally ill patients' wishes, research is needed on clinically modifiable factors that facilitate or impede preferred-received LST concordance at EOL. Such evidence would guide development of effective interventions to facilitate value-concordant EOL care.

Hence, this secondary analysis study was undertaken to examine the effectiveness of our blinded RCT[18] of an individualized, interactive ACP intervention (protocol in Appendix I) in facilitating concordance between terminally ill cancer patients' preferred and received LST states and to explore modifiable factors facilitating or impeding such concordance.

Methods

Overview

This ACP intervention sought not only to improve concordance between patients' preferred and received EOL care but also to improve quality of life (QOL), lessen depressive and anxiety symptoms of patients and caregivers during the patient's dying process, and enhance family caregivers' bereavement adjustment. This intervention was shown to improve terminally ill cancer patients' psychological symptoms (a primary outcome), but not their QOL and concordance (two primary outcomes) between preferred and received individual LSTs.[18] The ACP intervention's facilitation of two secondary outcomes (accurate prognostic awareness early in participants' terminal illness trajectory and reduced cardiopulmonary resuscitation [CPR] received in the last month) has been reported.[19] Herein, we reexamined our intervention's facilitation of concordance between patients' states of preferred and received LSTs (hereafter called preferred-received LST-state concordance). Of note, this concordance was not preidentified as a secondary outcome. We used advanced statistics (see Statistical Analysis) to identify preferred and received LST states and modifiable factors facilitating or impeding preferred-received LST-state concordance.

Design, Setting, and Sample

Methodological details and sample characteristics of our ACP RCT have been reported.[18] A consecutive sample of 460 terminally ill cancer patients was randomly assigned 1:1 to the experimental (transtheoretical model-based, tailored, multifaceted, interactive intervention) and control (sham treatment of symptom-management education) arms.[18] The experimental arm received an ACP intervention with the following components: 1) repeated assessments and provision of subinterventions tailored to participants' readiness to engage in ACP; 2) facilitating physician-patient EOL-care discussions; 3) use of a workbook and a video educational aid to facilitate understanding of ACP and LSTs at EOL; and 4) psychologically supporting participants while engaged in EOL-care decision making. Treatment fidelity was highly ensured.[18,19] The final sample comprised 430 participants who died through December 2017 (CONSORT diagram in Fig. 1). Between-arm homogeneity in baseline characteristics, LST preferences, accurate prognostic awareness, physical and psychological symptoms, and QOL were verified for the study arms
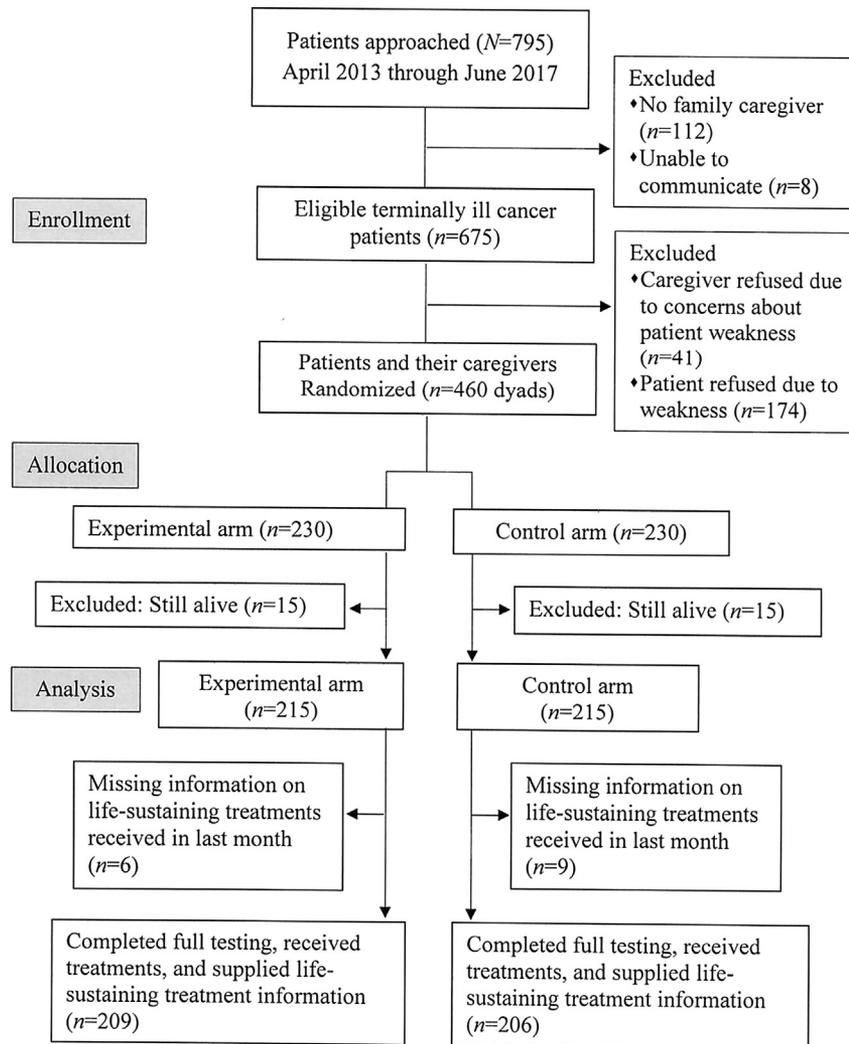
Fig. 1. Consort diagram.

at the start and end of the study.[18,19] The sample was predominantly male (68.4%−72.6%) and 25.1% −29.3% were >65 years old. Median follow-up to participant death was 79−86 days (mean [SD] = 127.39−147.33 [151.66−155.01]). About one-fourth of participants (23.9%) did not know their prognosis throughout their dying process, with 28.4%, 21.7%, and 26.0% of participants first reporting accurate prognostic awareness 1−60, 61−180, and >180 days before death, respectively.[18,19] The original study was approved by the ethics committee of the study site (101-0898A3) and registered at ClinicalTrials.gov (NCT01912846). All participants provided written informed consent before enrollment.

Outcome Measures
Preferences for Life-Sustaining Treatments. We assessed preferences for CPR, intensive care unit (ICU) care, chest compression, intubation with mechanical

ventilation, nasogastric tube feeding, and intravenous nutrition using an adapted interview protocol (Appendix II). For each LST, patients were asked whether they 1) wanted, 2) did not want, or 3) were undecided about the treatment. We retained "undecided" as a valid response in contrast to the common approach of dichotomizing EOL-care preferences into "want"/"do not want" treatment[20,21] with those indicating "undecided" counted as wanting that treatment. The primary reason for our approach was that decisional uncertainty may reflect patients' lack of knowledge about and understanding of the clinical situation or the risks and benefits inherent in each EOL-care decision, and their inability to project their preferences into the future,[22] especially for unknowable situations[23] such as one's death and dying. Categorizing "undecided" responses as treatment preferences may have inflated preference rates, but removing them from analyses may not bring undecided patients' preferences to the attention of clinicians, who would

miss the opportunity to meet these patients' needs at EOL.

Life-Sustaining Treatments Received. Data on the aforesaid six LSTs received in patients' last month were retrieved from medical records. When these data were missing from medical records, they were obtained from caregivers' reports during bereavement follow-ups.

Preferred-Received LST-State Concordance. The outcome variable was preferred-received LST-state concordance, with estimations based on collected data (see Data Collection) and cross-tabulation (see Statistical Analysis).

Modifiable Time-Varying Factors Facilitating or Impeding Preferred-Received LST-State Concordance

We examined potential factors (physical symptom distress,[24] functional dependence,[25] and prognostic awareness[24]) facilitating or impeding preferred-received LST-state concordance for terminal patients and modifiable by effective palliative care.[26–28] We also examined anxiety and depressive symptoms[16,29,30] and QOL[29,31] as potential predictors of concordance based on their documented associations with EOL-care preferences. Time-varying factors that might facilitate or impede preferred-received LST-state concordance were adjusted to account for different subject-specific responses experienced at different times.[32,33] All instruments selected for time-varying, clinically modifiable variables have been validated by the original developers and extensively used in the principal investigator's research to test hypothesized relationships between concepts measured.[34–36]

Physical symptom distress was measured by the 13-item Symptom Distress Scale,[37] which assesses cancer patients' common symptoms (e.g., pain, dyspnea, anorexia, and insomnia). Score range = 13–65; higher scores indicate greater distress.

Functional dependence was measured by the 10-item Enforced Social Dependency Scale.[38] Score range = 10–51; higher scores reflect greater dependence on help for personal and social functioning.

Prognostic awareness was evaluated by asking patients if they knew their prognosis, and if so, whether their disease 1) was curable; 2) might recur in the future, but their life was not currently in danger; or 3) could not be cured, and they would probably die in the near future.[34,36] Only patients who chose Option 3 were recognized as accurately understanding their prognosis. Our measure of accurate prognostic awareness, that is, "understanding that one's disease is incurable, life-threatening, or death is

approaching," maps onto the conceptualization of prognostic awareness commonly adopted in the literature.[39] To determine preferred-received LST-state concordance (see Statistical Analysis), we used accurate prognostic awareness when it was first reported by participants in reference to time proximity to death (the period between death and assessment, i.e., 1–60, 61–180, >180 days before death).

Anxiety and depressive symptoms were measured by the Hospital Anxiety and Depression Scale (HADS).[40] The 14-item HADS, the most widely used tool for assessing psychological distress in palliative cancer patients,[41] assesses psychological rather than physiological symptoms, thus avoiding confounding measures that may overestimate anxiety or depression severity for cancer patients who commonly suffer from multiple physical symptoms. The HADS-A and HADS-D subscales measure anxiety and depressive symptoms, respectively. Each seven-item subscale has a total score ranging from 0 to 21; higher scores indicate more anxiety or depressive symptoms.

Quality of life was measured by a modified 13-item McGill Quality of Life Questionnaire (MQOL).[42] The original MQOL stresses psychological, social, and existential well-being. The MQOL was modified by omitting three items for the most distressing symptoms to avoid overlap with the known effect of symptom distress on QOL but retaining the item for evaluating overall physical well-being. Total scores for this modified MQOL range from 0 to 130; higher scores indicate better QOL.

Covariate Measures

We adjusted for treatment dose (number of intervention-treatments provided) and time-invariant variables (age and gender) as covariates of preferred-received LST-state concordance.

Data Collection

Participants' characteristics were assessed at baseline (before random assignment). Data on LST preferences and time-varying factors were collected by experienced, trained oncology nurses at baseline and every three to four weeks afterward until participants declined participation or died. Data collectors were blinded to participants' group assignment.[18]

Statistical Analysis

LST-preference states were estimated over participants' last six months, and received LST states were estimated in their last month. A transition model with hidden Markov modeling (HMM)[43] was used to simultaneously identify distinct LST-preference states and examine probabilities of shifting from

one state to another between consecutive time points (transition probability) using Latent GOLD 5.0 (Groningen, Netherlands). Detailed procedures for identifying the optimal number of distinct LST-preference states and estimating transition probabilities are in Appendix III.

LST states received in patients' last month were identified using the same procedures described in Appendix III, except those for estimating state-transition probabilities. Concordance was evaluated by cross-tabulating preferred LST states estimated just before death (Appendix III) and LSTs received in the last month. Concordance is expressed both as a percentage (received/preferred LSTs) and as a kappa coefficient for chance-corrected agreement.[44] Concordance (kappa value) was determined as poor (≤0.20), fair (0.21−0.40), moderate (0.41−0.60), substantial (0.61−0.80), or almost perfect (0.81−1.00).[45]

Effectiveness of our ACP intervention on and factors facilitating or impeding preferred-received LST-state concordance was identified by multivariate logistic regression. We examined the effect of our ACP intervention on preferred-received LST-state concordance by its main effect and interactions with accurate prognostic awareness[22] when it was first reported relative to death based on our hypothesis (Appendix I) that facilitating patients' development of accurate prognostic awareness earlier in the terminal-illness trajectory would allow them sufficient time to consider their EOL-care goals and prepare, emotionally and practically, for their EOL-care decision making, thereby improving preferred-received LST-state concordance. We also modeled preferred-received LST-state concordance as a function of proposed lagged time-varying predictors (symptom distress, functional dependence, anxiety symptoms, depressive symptoms, and QOL) in the last wave of assessment while controlling for time-invariant variables (age and gender) and treatment dose. The lagged measure was added to identify variables facilitating or impeding preferred-received LST-state concordance by arranging time-varying, modifiable independent variables (measured in the last wave of assessment before death) and the outcome variable in the closest time sequence to ensure the strongest impact of the proposed independent variables. The regression parameter for each independent variable was exponentiated to transform into adjusted odds ratio (AOR) with 95% CI. Because our approach to identifying factors facilitating or impeding preferred-received LST-state concordance was exploratory, we did not adjust the significance level for comparing multiple independent variables in our multivariate analysis model but set it at $P \le 0.05$.

Table 1
Emission Probabilities and Initial Sizes of the Three States of Preferences for Life-Sustaining Treatments
($N = 425$)

	State 1	State 2	State 3
	Initial Size (%)		
Preferences for Life-Sustaining Treatments	38.0	50.5	11.5
Want treatment			
Cardiopulmonary resuscitation	**0.998**	0.001	0.026
Intensive care unit care	**0.998**	0.051	**0.481**
Chest compression	**0.992**	0.002	0.070
Intubation with mechanical ventilation	**0.964**	0.000	0.013
Nasogastric tube feeding	**0.987**	0.279	**0.760**
Intravenous nutrition support	**1.000**	0.711	**0.906**
Don't want treatment			
Cardiopulmonary resuscitation	0.002	**0.993**	0.475
Intensive care unit care	0.002	**0.949**	0.080
Chest compression	0.008	**0.998**	**0.567**
Intubation with mechanical ventilation	0.036	**1.000**	**0.643**
Nasogastric tube feeding	0.013	**0.705**	0.040
Intravenous nutrition support	0.000	0.287	0.000
Undecided			
Cardiopulmonary resuscitation	0.000	0.006	**0.499**
Intensive care unit care	0.000	0.000	0.438
Chest compression	0.000	0.000	0.363
Intubation with mechanical ventilation	0.000	0.000	0.345
Nasogastric tube feeding	0.000	0.016	0.200
Intravenous nutrition support	0.000	0.002	0.094

Among 430 participants, five were excluded because they were only assessed six months or more before death.
Bold values indicates the emission probabilities for participants in each state wanting, rejecting, and being undecided about each treatment. For example, participants in State 3 had 0.481, 0.760, and 0.906 probabilities of wanting intensive care unit care, nasogastric tube feeding, and intravenous nutrition support, respectively, with 0.567 and 0.643 probabilities of rejecting chest compression and intubation with mechanical ventilation support, respectively, and 0.499 probability of uncertainty about cardiopulmonary resuscitation.

Results

Preferred and Received LST States and Transitions Between LST-Preference States in Participants' Last Six Months

Model fit indexes for the one- through five-state HMM solutions of LST preferences are in Appendix IV. Evaluation of model fit indexes, information-criterion plots (Appendix VI), and clinical meaningfulness supports selection of a three-state solution for LST preferences as optimal and parsimonious. These states, whose emission probabilities and sizes (state probabilities) are in Table 1, were labeled uniformly preferring LSTs, rejecting LSTs except intravenous nutrition support, and mixed LST preferences. When LST preferences were initially assessed on average four to five months before death (see Design, Setting, and Sample), the most prevalent state was rejecting LSTs except intravenous nutrition support (State 2, 50.5%) (Table 1), followed by uniformly preferring LSTs (State 1, 38.0%). About one-tenth

	State 1	State 2	State 3
	Initial Size (%)		
Life-Sustaining Treatments Received in the Last month	5.0	89.3	5.8
Treatment received			
Cardiopulmonary resuscitation	**0.979**	0.000	0.115
Intensive care unit care	**0.551**	0.008	**0.903**
Chest compression	**0.961**	0.000	0.048
Intubation with mechanical ventilation	**0.792**	0.000	**0.985**
Nasogastric tube feeding	**0.684**	0.280	**0.920**
Intravenous nutrition support	**0.805**	**0.849**	**0.998**
Treatment not received			
Cardiopulmonary resuscitation	0.021	**1.000**	**0.885**
Intensive care unit care	0.449	**0.992**	0.097
Chest compression	0.039	**1.000**	**0.953**
Intubation with mechanical ventilation	0.208	**1.000**	0.015
Nasogastric tube feeding	0.316	**0.720**	0.080
Intravenous nutrition support	0.195	0.151	0.002

Bold values indicates the emission probabilities for participants in each state receiving or not receiving each treatment.

(11.5%) of participants preferred ICU care and nutrition support (by intravenous or nasogastric tube feeding) but declined chest compression and intubation with mechanical ventilation and were undecided about CPR.

The transition probabilities for participants in a specific state moving between states from time t−1 to time t showed that LST preferences were highly stable between consecutive assessments, as evident by most LST-preference states (95.7% to 99.5%; bolded in Appendix VIII) remaining in their original state rather than shifting to another state. Ranking of the last assessed LST-preference states did not differ from initial preferences, but the prevalence of States 1 (uniformly preferring LSTs), 2 (rejecting LSTs except intravenous nutrition support), and 3 (mixed LST preferences) decreased (38.0% to 25.2%), increased (50.5% to 62.6%), and was nearly unchanged (11.5% to 12.2%), respectively.

HMM identified three LST states received by participants in their last month (Appendices V and VII), with their emission probabilities and sizes (Table 2). These three states were identified as uniformly receiving LSTs (State 1), receiving intravenous nutrition only (State 2), and selectively receiving LSTs (State 3, receiving ICU care, intubation with mechanical ventilation, and nutrition support [by intravenous or nasogastric tube feeding] but withholding CPR and chest compression). The most prevalent received LST state was receiving intravenous nutrition only (State 2, 89.3%). Few participants received all (State 1, 5.0%) or selected (State 3, 5.8%) LSTs in their last month.

Preference for Life-Sustaining Treatments	Life-Sustaining Treatments Received			
	State 1	State 2	State 3	Total
Experimental arm				
State				
1	**4**	44	5	53
2	3	**119**	6	128
3	2	18	**5**	25
Total	9	181	16	206
Concordance, %	62.14			
Kappa (95% CI)	0.126 (0.032, 0.221)			
Control arm				
State				
1	**3**	44	3	50
2	4	**123**	4	131
3	3	20	**1**	24
Total	10	187	8	205
Concordance, %	61.95			
Kappa (95% CI):	0.050 (−0.028, 0.128)			
Arm difference				
Odds ratio (95% CI)	1.008 (0.675, 1.5001)			

Preferred life-sustaining treatment (LST): State 1: uniformly preferring LSTs; State 2: rejecting LSTs except intravenous nutrition support; State 3: mixed LST preferences.
LSTs received: State 1: LSTs uniformly received; State 2: receiving intravenous nutrition only; State 3: selected receipt of LSTs (i.e., received intensive care unit [ICU] care, intubation with mechanical ventilation, nutrition support with cardiopulmonary resuscitation [CPR], and chest compression withheld). Bold indicates numbers of patients with concordant preferred and received LST states.
For patients with mixed LST preferences (State 3) estimated at their last assessment, preferred and received LST states were concordant when patients' wishes were predominantly honored, that is, they received preferred LSTs (ICU care and nutrition support), and declined (chest compression) or undecided LSTs (CPR) were withheld in the last month because clinicians judged CPR as futile.

ACP Intervention Effectiveness in Facilitating Preferred-Received LST-State Concordance

The concordances between experimental-arm and control-arm patients' preferred and received LST states (Table 3, bolded values) were 62.14% and 61.95%, respectively. Between-arm concordant/discordant preferred-received LST-state patterns were similar. LST preferences were most honored for participants who rejected LSTs except intravenous nutrition support (93.0%−93.9%; 119/128 and 123/131 for the experimental and control arms, respectively; Table 3). Fewer than one-tenth (6.0−7.6%; 4/53 and 3/50) of experimental-arm and control-arm participants, respectively, who uniformly preferred LSTs received them, whereas the majority of participants in preferred States 1 and 3 received intravenous nutrition support only (44/53 and 18/25, respectively, for the experimental arm, and 44/50 and 20/24, respectively, for the control arm). Among participants who preferred intravenous nutritional support only (preferred State 2), 6.1%−7.0% (8/131−9/128) received all or some LSTs such as ICU care, CPR, and intubation with mechanical ventilation support (received State 1 or 3, respectively).

Table 4
Factors Facilitating Concordance Between States of Preferred and Received Life-Sustaining Treatments

Variable	AOR (95% CI)	P
Intercept	0.040 (0.003−0.506)	0.013
Arm		
Experimental	1.195 (0.512−2.793)	0.680
Control	Ref	
Accurate prognostic awareness relative to time proximity to death (days)		
1−60	4.574 (1.962−10.667)	<0.001
61−180	3.891 (1.645−9.202)	0.002
>180	8.108 (2.753−23.875)	<0.001
Never[a]	Ref	
Arm by accurate prognostic awareness relative to time proximity to death (days)		
Experimental × 1−60	0.723 (0.222−2.352)	0.590
Control × 1−60	Ref	
Experimental × 61−180	0.593 (0.169−2.082)	0.415
Control × 61−180	Ref	
Experimental × >181	0.487 (0.135−1.755)	0.272
Control × >181	Ref	
Experimental × never	Ref	
Control × never	Ref	
Symptom distress	1.032 (0.998−1.066)	0.064
Functional dependence	0.992 (0.959−1.027)	0.659
Quality of life	1.018 (1.000−1.036)	0.049
Anxiety symptoms	0.895 (0.823−0.972)	0.009
Depressive symptoms	1.109 (1.009−1.219)	0.033
Gender		
Male	0.911 (0.564−1.469)	0.701
Female	Ref	
Age	0.996 (0.976−1.017)	0.725
Treatment dose	0.991 (0.946−1.038)	0.701

AOR = adjusted odds ratio; Ref = reference.
[a]Participants who never reported accurate prognostic awareness.

The preferred-received LST-state concordances of the experimental and control arms were comparable (kappa [95% CI]: 0.126 [0.032, 0.221] vs. 0.050 [-0.028, 0.128]), with a nonsignificant difference (OR [95% CI]: 1.008 [0.675, 1.500]) (Table 3). Between-arm comparability in the outcome variable was confirmed in multivariate logistic regression modeling (AOR [95% CI] = 1.195 [0.512, 2.793]; Table 4). Even after accounting for the interaction between study arm and accurate prognostic awareness, our ACP did not facilitate preferred-received LST-state concordance no matter how early prognosis was first accurately reported before the participant's death.

Modifiable Factors Facilitating or Impeding Preferred-Received LST-State Concordance

Important modifiable factors facilitating or impeding preferred-received LST-state concordance included prognostic awareness, QOL, and psychological distress but not symptom distress and functional dependence (Table 4). Participants who accurately knew their prognosis, regardless of how soon before death, were uniformly, significantly more likely to have their preferred LST states honored than those without accurate prognostic awareness throughout their dying process (AOR [95% CI] range = 3.891 [1.645, 9.202] to 8.108 [2.753, 23.875]). Preferred-received LST-state concordance was facilitated by better QOL (1.018 [1.000, 1.036]) and more depressive symptoms (1.109 [1.009, 1.219]) but was impeded by more anxiety symptoms (0.895 [0.823, 0.972]).

Discussion

In this secondary analysis study, terminally ill cancer patients' preferred and received LST states agreed poorly (0.050 [−0.028, 0.128] to 0.126 [0.032, 0.221]), and our ACP intervention did not increase the likelihood of participants' LST preferences being honored. However, preferred-received LST-state concordance was facilitated by accurate prognostic awareness, better QOL, and more depressive symptoms, but impeded by more anxiety symptoms. The poor preferred-received LST-state concordance and the inability of our ACP intervention to honor participants' LST preferences echo the literature[9,12] and may be due to our study being underpowered to explore this outcome. We did not estimate our sample size based on effect sizes from ACP RCTs for cancer patients because such RCTs were not published when we launched our study. The poor preferred-received LST-state concordance primarily resulted from participants not receiving aggressive LSTs as they preferred. This poor concordance may reflect Taiwan's current hospice movement, which influences clinicians to provide less aggressive care than patients prefer to avoid suffering futile and costly LSTs, thus benefiting both patients and society at large. This system-wide philosophy and these practices may have impeded our ACP intervention in facilitating preferred-received LST-state concordance. Moreover, we repeatedly assessed participants' LST preferences over their dying process. This repeated assessment (testing)[46] may have threatened the internal validity of our study by sensitizing and motivating control-arm participants to prepare for their EOL care, thereby neutralizing or minimizing the intervention's effectiveness in facilitating concordance between patients' preferred and received LSTs.

Accurate prognostic awareness significantly facilitated participants' preferred-received LST-state concordance regardless of when in the dying trajectory they first knew their prognosis. Our finding on accurate prognostic awareness not only confirms the conclusion that this awareness ensures that terminally ill cancer patients receive EOL care consistent with their preferences[24] but also goes a step further by indicating that accurate prognostic awareness per se is valuable for value-concordant EOL care despite a

suggestion that some patients know their prognosis too late in the disease trajectory to appropriately discuss/prepare for EOL care.[47]

Our study contributes the novel findings that terminally ill cancer patients' preferred-received LST-state concordance is associated with QOL and psychological distress. Better QOL facilitated our participants' preferred-received LST-state concordance. Improved QOL has been associated with less willingness to risk severe suffering to receive LSTs, leading to fewer LST preferences.[29,48] Enjoying better QOL reassures terminally ill cancer patients that the *status quo* is good enough not to undergo the unnecessary suffering caused by additional LSTs. Indeed, participants who reported better QOL in the last assessment were more likely to be in LST-preference State 2 (rejecting LSTs except intravenous nutrition support, data not shown) and to have their preferences for rejecting LSTs honored (as shown by >90% of State 2 participants eventually achieving their LST preferences). Similarly, our participants with more depressive symptoms tended to forgo LSTs (as in LST-preference State 2, data not shown), as reported for older adults and patients with advanced disease,[29,30,49] probably due to despair about the future leading them to give up fighting their disease via LSTs. These participants were also highly likely to receive EOL care without aggressive treatments, consistent with their wishes. By contrast, participants with more anxiety symptoms might seek LSTs (as in LST-preference States 1 or 3, data not shown) to combat their progressive disease and their increasing vulnerability as they face death. Given the futility of LSTs in prolonging life at EOL, their LST preferences were highly likely to be denied, leading to discordance in their preferred and received LSTs. However, this hypothesis warrants further validation, preferably by qualitative studies because more anxiety symptoms have been associated with a change from preferring to rejecting LSTs.[29]

Study Limitations

The generalizability of our findings to national and international target populations may have been compromised by convenience sampling patients with a family caregiver from a single Taiwanese hospital. Our findings from Taiwan need to be replicated for terminally ill cancer patients in other countries where cultural, societal, and health care characteristics may substantially differ, especially for our identification of distinct preferred and received LST states and the novel associations of patients' QOL and psychological distress with preferred-received LST-state concordance. Furthermore, our study was limited by not adjusting our multivariate analysis for multiple comparisons of independent variables. Our

investigation into LST-preference states was limited to the six LSTs assessed. We focused on patient participants and have not yet considered family caregivers' perspectives.[50] Future studies should evaluate how family caregivers' understanding and endorsement of patients' LST preferences in the context of ACP interventions facilitate patient-family concordance on LST-preference states to achieve patient value-concordant EOL care.

Conclusion and Clinical Implications

Our ACP intervention did not improve concordance between terminally ill cancer patients' preferred and received LST states. However, preferred-received LST-state concordance was facilitated by patient-reported accurate prognostic awareness, better QOL, and more depressive symptoms, whereas this concordance was impeded by more anxiety symptoms. To facilitate patient value-concordant EOL care and help terminally ill cancer patients achieve a good death,[1] interventions should be developed and implemented to cultivate these patients' accurate prognostic awareness, maximize their QOL,[26–28] support depressive patients' values and sense of humanity while endorsing their wishes to forgo LSTs, and clarify anxious patients' misunderstanding or unrealistic expectations of LST efficacy at EOL.[51,52]

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Appendix I

Study Protocol

Title: An Interactive Advance Care Planning Intervention to Facilitate a Good Death for Cancer Patients

Brief summary: The purpose of this five-year intervention study is to design, implement, and evaluate the effectiveness of an intervention aimed at facilitating prognostic communication and end-of-life (EOL) care decision making to increase congruence between patients' preferred and received EOL care, improve patients' and family caregivers' quality of life (QOL) and psychological well-being, reduce utilization of futile aggressive health care resources at EOL, and facilitate bereavement adjustment.

Detailed description: A randomized controlled trial (RCT) of a tailored, multifaceted intervention will be conducted on a consecutively recruited sample of 231 dyads of terminally ill cancer patients and their family caregivers. Intervention effectiveness will be evaluated by comparing outcomes between patient-caregiver dyads in the experimental arm and the same number of dyads in a symptom-management education control arm.

The primary objectives are to examine the extent to which the proposed advance care planning (ACP) intervention will 1) increase congruence between terminally ill cancer patients' preferred and received end-of-life (EOL) care, 2) improve quality of life (QOL) and reduce patients' and caregivers' depressive and anxiety symptoms during the patient's dying process, and 3) enhance family caregivers' bereavement adjustment.

The secondary objectives are to determine the effectiveness of the proposed ACP intervention in facilitating patients' prognostic awareness and EOL-care discussions among patients, families, and physicians; in increasing patient-caregiver agreement on EOL-care preferences; and in reducing aggressive EOL-care treatments for terminally ill cancer patients.

Sample size calculation: Sample size will be estimated based on observational evidence that EOL-care discussions between terminally ill cancer patients and their physicians increase congruence between patients' preferred and received EOL care.[1] This evidence was used because no intervention to date has been shown to directly increase congruence between terminal cancer patients' preferred and received EOL care. Patients who reported having EOL-care discussions with their physicians were more likely than those who did not have such discussions to receive EOL care consistent with their preferences (odds ratio [OR] = 2.04; $P < 0.0001$)[1] and received significantly fewer aggressive medical interventions near death, with lower rates of cardiopulmonary resuscitation (0.8% vs. 6.7%; adjusted odds ratio [AOR], 0.16; 95% CI, 0.03−0.80), mechanical ventilation support (1.6% vs. 11.0%; AOR, 0.26; 95% CI, 0.08−0.83), and intensive care unit (ICU) care (4.1% vs. 12.4%; AOR, 0.35; 95% CI, 0.14−0.90), respectively. A sample of 124−190 dyads per arm would achieve 85% power to detect a between-arm difference in patient-physician EOL-care discussions by two-sided tests with $P < 0.05$. To compensate for the 18.5% attrition rate found in our previous longitudinal study,[2] 147−231 dyads per arm are needed. The proposed sample will target 231 dyads per arm to ensure adequate power to detect the hypothesized effects of the proposed intervention.

Participant recruitment: Terminally ill cancer patients will be consecutively referred by their participating oncologists by these criteria: 1) diagnosed with a terminal-stage disease that continues to progress with distant metastases and judged by their oncologists as unresponsive to current curative cancer treatment, 2) cognitively competent, 3) able to communicate with data collectors, 4) age>20 years, and 5) having a designated family caregiver who agrees to participate.

Family caregivers will be recruited if they 1) are family members of cancer patients with a terminally ill disease as defined by this proposed study, 2) are identified by patients as the primary person caring for them without financial reimbursement for that care, 3) are aged >20 years, and 4) agree to participate and can communicate with data collectors. Patients and family caregivers will be excluded if they participate in other research to facilitate prognostic awareness, ACP, QOL, or psychological well-being.

Detailed information about patients' eligibility criteria will be given to patients' oncologists who agree to participate in this study. They will be asked to identify and refer all dyads of patients and family caregivers without judging their emotional readiness to talk about their prognosis and EOL-care preferences. Referred patients' and caregivers' eligibility will be evaluated by data collectors who will invite them to participate in the study. Because QOL, depressive symptoms, and anxiety symptoms for both patients and family caregivers are primary study outcomes, patient-caregiver dyads will be excluded if either the patient or caregiver cannot communicate with the data collectors or refuses to participate.

Approximately eight to 10 new dyads of terminally ill cancer patients and their family caregivers will be recruited each month. After developing a detailed study protocol, we will recruit the targeted 462 participant dyads (231 dyads in each treatment arm). We will enroll and randomly assign eligible patient-caregiver dyads 1:1 to the intervention or attention-control arm without stratification.

ACP intervention: The goal of this theory-based, tailored, multifaceted, interactive ACP intervention is to facilitate discussions among terminally ill cancer patients, their family caregivers, and their primary physicians about the patient's EOL-care preferences and to honor the patient's wishes. To that end, the ACP intervention will clarify each participant's understanding of the patient's prognosis and treatment options and her/his readiness to engage in ACP, help participants appropriately weigh the benefits and burdens of medical treatments at EOL, and clearly define and document the patient's preferences for their oncologist to use later to guide EOL-care decision making that honors the patient's preferences. The intervention constitutes dynamic and multiple interactions between patients, family caregivers, and primary physicians and a trained, master's prepared ACP interventionist with experience in oncology nursing and palliative care. The ACP interventionist will use two decision aids (a booklet and a video) to enhance participants' understanding of the essential elements in ACP and aggressive EOL care.

The major components of the proposed ACP intervention will include 1) repeated assessments of participants' readiness to engage in ACP; 2) specific interventions tailored to participants' readiness to engage in ACP; 3) facilitating prognostic communication and EOL-care discussions among patients, family caregivers, and physicians; and 4) use of a booklet and a video educational aid to facilitate understanding of ACP and life-sustaining treatments at EOL.

The trained ACP interventionist will begin each course of the ACP intervention by independently and separately assessing each patient's and family caregiver's readiness to engage in ACP. The ACP interventionist will assess participants' understanding of how the illness is likely to progress, EOL-care preferences and goals, and readiness to engage in ACP. "Course" refers to each repetition of the four major intervention components. Each course will assess participants' readiness for ACP and EOL-care preferences to determine if they have changed over time and to adjust the intervention accordingly. The participant's stage of readiness to engage in ACP will be determined according to the Transtheoretical Model.[3] For this study, we propose that in the first stage, precontemplation, the participant is unaware of the prognosis or has no desire to engage in ACP planning. In the second stage, contemplation, the participant understands the relevance of ACP to his/her life and begins to consider his/her values and future treatment preferences. In the third stage, preparation, the participant commits to engage in ACP soon but is not yet ready to do so. In the fourth stage, action, the participant overtly engages in ACP, for example, discusses and clarifies his/her EOL-care preferences with family members and health care professionals. In the fifth stage, maintenance, the participant has made EOL-care decisions and can periodically evaluate these decisions given changes in her/his life status.

The intervention protocol in this trial will not follow a script for discussing prespecified topics. Rather, the trained ACP interventionist will have the flexibility to provide participant-centered care tailored to the participant's specific needs at each stage of readiness to engage in ACP. For participants in the precontemplation stage, the goal of the individualized intervention will be to address participants' lack of readiness to engage in ACP and to motivate them to think of the relevance of ACP. For participants in the contemplation stage, the ACP interventionist will discuss life-sustaining treatments and palliative care that may be applicable to that patient, explain the benefits and burdens of each treatment, and encourage patients and caregivers to evaluate these benefits and burdens from their own perspective. For participants in the preparation stage, the ACP interventionist will help them to determine specific EOL-care preferences and to communicate their preferences and concerns to primary physicians. For participants ready to act on ACP, the ACP interventionist will communicate patients' and family caregivers' EOL-care preferences to their oncologist, thus facilitating EOL-care discussions to achieve a consensus on EOL-care goals and specific treatments that could be used or withheld. For participants who have made EOL-care decisions, the ACP interventionist will continually support and reassure them that their goals and EOL-care plan will be periodically reviewed based on changes in the patient's health status and preferences.

To enhance consensus in perceptions of the prognosis and EOL-care goals/preferences among terminally ill cancer patients, their family caregivers, and physicians, the ACP intervention protocol is designed to facilitate discussions about these topics throughout the dying process. Because patients' preferences and concerns fluctuate over the dying process, a basic tenet of this intervention is that ACP will be revisited periodically to ascertain any changes in participants' values regarding an acceptable QOL and desirable EOL care as the patient's death approaches. After the initial intervention course, the ACP interventionist will interact with participants at least every month until the patient dies. If the patient's health status declines as assessed by the primary physician or the patient experiences sentinel events, for example, initiating a new chemotherapy regimen, deciding to undergo major surgery, admission to an ICU, initiating mechanical ventilation or new hemodialysis, and diagnosis with central nervous system metastases, the next intervention course will be scheduled immediately to readdress the participant's EOL-care goals and preferences. The tailored intervention will be provided according to the patient's specific needs.

The symptom-management educational control arm is designed to compare the effects of the multifaceted, interactive ACP intervention to those of a symptom-management educational intervention to rule out the Hawthorne effect. The control-arm protocol will include prognostic disclosure and EOL-care discussions as needed according to current clinical practice. This study arm will be provided by treatment providers who are trained, master's degree−prepared nurses with experience in oncology nursing and palliative care. In the initial session for this arm, the treatment provider will give terminally ill cancer patients and family caregivers a booklet and a video with educational materials on how to manage common symptoms and a list of available resources, including patient support organizations, as well as support and financial assistance through the hospital's social work department. We hypothesize that using a booklet and video on symptom management alone will not impact the outcomes but will parallelize education received by the control arm as much as possible with that of the experimental arm. This hypothesis is based on a systematic review that found using informative material alone did not promote use of ACP.[4] The control-arm treatment provider will visit and interact with control-arm participants according to the same schedule as for the experimental arm (weekly during hospitalization or monthly at outpatient visits until they die) to assess their symptom distress and general well-being. Necessary referrals to physicians or social workers will be made for further management.

Data collection procedures: Participants will be assessed prospectively until patient death, loss to follow-up, study withdrawal, or when the patient can no longer be interviewed. Both patients and their family caregivers will be assessed every three weeks for QOL and other outcomes to cover the most rapid changes in patients' physical condition and demanding period of caregiving until the patient's death.[5] After each patient's death, his/her chart will be reviewed, and his/her caregiver will be interviewed to confirm the type of medical care received at EOL. At one, three, six, and 13 months after the patient's death, bereaved family caregivers will be interviewed. Thirteen months was chosen instead of 12 months to avoid contamination with effects based on anniversary grief reactions.[6]

Several strategies will be taken to ensure research fidelity.

1. Training of the treatment providers:
   The proposed ACP intervention requires professionals skilled in the content, techniques, and delivery of the intervention. The interventionist will be trained using competency-based education based on her previous oncology and hospice care experiences. The training will include an overview of the study protocol and procedures, a review of the developed booklet and video, and instructions in motivational assessments. The interventionist will be coached by the principal investigator (PI), who will serve as a role model, to assess and motivate participants at different stages of readiness for engaging in ACP and cooperating with physicians to coordinate and facilitate EOL-care discussions. Before formal interventions can proceed, the interventionist will need to successfully demonstrate predefined competencies and consistency in delivering the ACP intervention after training and receiving individual feedback from the PI. Thereafter, the study team will meet biweekly to review the interventionist's notes on intervention sessions and to provide feedback on difficult participant-management issues.
   The control-arm treatment provider will be trained by the PI to understand the purposes of this symptom-management educational treatment, how to assess common symptoms for terminally ill cancer patients, and how to use the booklet and video to help terminally ill cancer patients and their family caregivers manage the patient's symptom distress. During training, the treatment provider will receive individual feedback from the PI. Before the treatment provider can formally provide symptom-management educational treatment, she will need to successfully demonstrate competencies and consistency in delivering the treatment. Thereafter, the study team will meet periodically to review the treatment provider's notes on symptom-management educational treatment sessions and to provide feedback on difficult participant-management issues.
2. Interventions provided to experimental-arm participants will be compared every three months with those received by control-arm participants. Randomly selected patient-caregiver dyads in each treatment arm will be interviewed by the PI to check the extent to which treatments provided to them are consistent with the protocol for each arm.
3. To avoid bias, separate data collectors will be hired and trained to independently collect data for the experimental and control arms. These research assistants (RAs) will be blinded to treatment condition and trained to screen participants, obtain consent, and administer the project instruments without offering information. Procedures will be implemented to ensure that data collection is standardized. RAs' reliability will be established by comparing data collected by the RAs with that recorded by the PI on five pilot cases. PI-RA agreement must be 95% before RAs can collect data for the main study. Failure to reach this agreement rate will require additional training until the reliability level is acceptable. To maintain 95% PI-RA agreement, the PI will check reliability intermittently throughout the study.
4. To ensure continuing patient safety as well as the validity and scientific merits of the trial, an independent Data and Safety Monitoring Board (DSMB) will be organized. The DSMB will constitute a biostatistician experienced in statistical methods for clinical trials, a nurse researcher experienced in conducting RCTs, and a physician-scientist experienced in cancer care.

The DSMB will monitor and address the following issues: 1) sufficient and appropriate enrollment of participants, including compliance with the eligibility criteria for each dyad of terminally ill cancer patients and family caregivers enrolled in the trial, 2) appropriate implementation of randomization, 3) comparability of baseline

data between treatment arms, 4) protocol compliance, including treatments delivered to each treatment arm and data collection schemes, 5) adverse events (AEs), quality assurance for data validation, and registry procedures for Clinical Trial registration at ClinicalTrials.gov.

Treatments delivered to participants assigned to the intervention and symptom-management education arms will be compared every six months by interviewing randomly selected patient-caregiver dyads in each treatment arm to check treatment components provided to them.

The study team will record AEs and submit them in writing to the DSMB monthly, with immediate reporting of serious AEs to the DSMB and an oncologist with expertise in cancer care. Site-reported AEs/SAEs to its institutional review board (IRB) will be dictated by local requirements.

No data will be analyzed before the study ends. Access to interim results, including results according to study arm, will be limited to DSMB members and the statistician who prepares the reports. The DSMB will review study data every six months, and the DSMB summary recommendations will be directed to the PI. A summary of the review of reported AEs/SAEs will be sent to the local IRB to ensure that the participating center will be informed of any pertinent safety issues.

The biostatistician will be responsible for ensuring quality of data submitted to the registry against the predefined range of each independent and dependent variable as well as for assessing the accuracy and completeness of registry data by comparing the submitted data to the original data.

Data analysis and interpretation:

1. All data will be scored and entered into a computer spreadsheet by an administrative assistant blinded to participants' arm allocation.
2. To test for baseline equivalence among participants in each arm, between-arm differences in baseline characteristics and identified outcomes will be assessed with two-sided Fisher's exact tests and chi-square tests for categorical variables and independent-sample Student's t-tests for continuous variables.
3. Intervention effectiveness will be examined using intention-to-treat regression analyses with generalized estimating equations (GEEs). In the intention-to-treat regression analyses, all patient participants will be analyzed in the treatment arm to which they are initially allocated until they die, regardless of whether they complete or withdraw from the treatment.
4. Congruence between terminally ill cancer patients' preferred and received EOL care will be determined by comparing agreement between EOL-care preferences elicited at the last assessment and EOL care received by the patient. Congruence will be expressed by the percentage of overall agreement and kappa coefficients to correct for the extent of agreement expected to occur by chance alone.
5. The impact of the intervention on congruence between terminally ill cancer patients' preferred and received EOL care and on secondary outcomes (prognostic awareness, EOL-care discussions, patient-caregiver agreement on EOL-care preferences, use of futile aggressive EOL care, hospice use, and early hospice referral) will be determined by multivariate logistic regression using GEE, while adjusting for confounding factors. We will also use the GEE model to examine the moderation effects of prognostic awareness, EOL-care discussions, and patient-caregiver agreement on EOL-care preferences on between-arm differences in congruence between terminally ill cancer patients' preferred and received EOL care, use of futile aggressive EOL care, hospice use, and early hospice referral.
6. Intervention effects on patients' and family caregivers' QOL and psychological well-being (anxiety and depression), as well as family bereavement outcomes (including QOL, depression, and grief reactions) will be examined by multivariate multiple regression using the GEE with simultaneous adjustment for confounding factors. We will also use the GEE model to examine the moderation effects of prognostic awareness, EOL-care discussions, and patient-caregiver agreement on EOL-care preferences on between-arm differences in patients' and family caregivers' QOL and psychological well-being before the patient's death, as well as family bereavement outcomes. The GEE model will also be used to examine how the intervention's effectiveness on patients' and family caregivers' QOL and psychological well-being before the patient's death and family bereavement outcomes will be moderated by aggressive EOL care and congruence between terminally ill cancer patients' preferred and received EOL care.

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Conceptual Framework
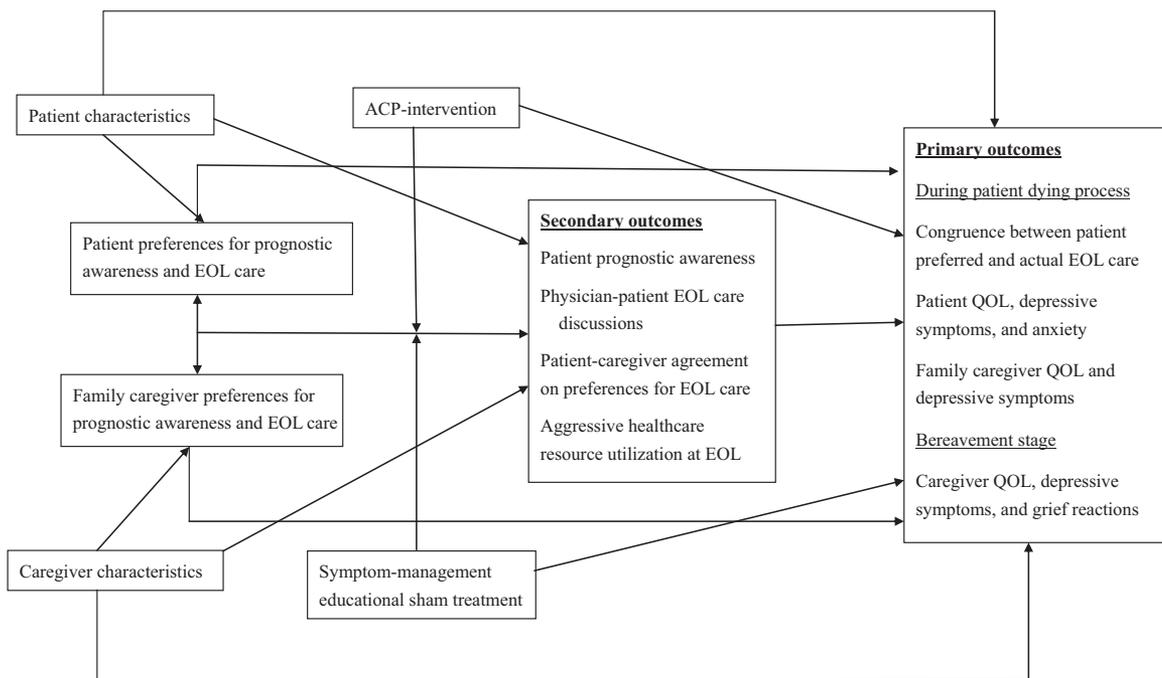
Appendix II

Interview Questions Regarding Preferences for Life-Sustaining Treatments

At the first interview, before participants were asked about their preferences regarding cardiopulmonary resuscitation (CPR), they were told, "If your heart were to stop beating and your life were in danger, your health care professionals might provide CPR. CPR consists of a combination of electric shocks to the heart, pumping the chest to stimulate the heart, placing a tube through a person's mouth or nose into their lungs and attaching this tube to a breathing machine to help with breathing, and heart medications given through the veins." Participants were then asked, "If your life was in danger, would you want to receive CPR?"

For life-sustaining treatments, participants were asked, If you were dying and

1. your heart stopped beating, would you want your chest to be pumped to stimulate the heart to beat?
2. If you were unable to breathe on your own, would you want to be intubated and on a breathing machine? In this situation, a tube would be placed through your mouth or nose into your lungs. This tube would be attached to a breathing machine. During that time, you would have to be continuously on the breathing machine and would be unable to talk and might be sedated.
3. If you need intensive care, would you like to stay in an intensive care unit (ICU)? An ICU is an isolated care unit that heavily uses health technology to provide intensive care and there is more nursing staff to closely monitor you. If you receive care in an ICU, you could only have contact with your family at specific visiting times.
4. If you cannot eat by yourself, would you be willing to be fed by artificial means, such as feeding through a nasogastric tube or receiving nutritional support by injection?

Adapted from Stapleton RD, Nielsen EL, Engelberg RA, Patrick DL, Curtis JR. Association of depression and life-sustaining treatment preferences in patients with COPD. Chest 2005; 127:328−334.

Appendix III

Transition Model With Hidden Markov Modeling to Identify Optimal Number of Distinct LST-Preference States and to Estimate Transition Probabilities

The first part of hidden Markov modeling (HMM)[1] assigned patients to a finite number of mutually exclusive probabilistic LST-preference states based on characteristics shared by patients in each state, thus discriminating them from patients in other states. Emission probability represented the observed probability that each patient would want, not want, or be undecided about each LST in each identified state, conditional on his/her state membership.[2] Model choice, in terms of the optimal number of states, was determined by examining fit indices with the Akaike information criterion (AIC),[3] the Bayesian information criterion (BIC),[4] the consistent AIC (CAIC),[5] sample size−adjusted BIC (SABIC),[6] and log-likelihood (LL).[7] Lower AIC, BIC, CAIC, and SABIC but higher LL scores generally indicate a better model fit. However, the flattening of information criterion (IC) values between consecutive numbers of hidden states in plots of IC values versus state number suggests that any increase in state number is not meaningful.[8] These criteria (i.e., generally lower IC and higher LL values, with more weight on flattening IC values between consecutive numbers of states), parsimony with adequate sample size,[9,10] and clinical meaningfulness of the identified state results were used to determine the optimal number of states. The second part of HMM estimated state-transition probabilities.[1] Transition probability represented the likelihood that a patient would prefer a specific set of LSTs at time t, given his/her preference for a specific LST set at time t−1. Based on each state's initial probability (size) and transition probabilities, we estimated each participant's last LST-preference state before death.

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Appendix IV
**Model Fit Indexes for One- to Six-State Solutions of Preferred Life-Sustaining Treatments**

State Number	Log Likelihood (LL)	BIC (LL)	AIC (LL)	CAIC (LL)	SABIC (LL)	Number of Parameters	Degrees of Freedom
1	−6865.11	13,802.84	13,754.22	13,814.84	13,764.76	12	13,302.44
2	−3532.04	7227.49	7118.08	7254.49	7141.81	27	6636.306
3	−2896.20	6058.69	5880.40	6102.69	5919.07	44	5364.626
4	−2433.09	5247.45	4992.17	5310.45	5047.53	63	4438.398
5	**−2257.69**	**5023.75**	**4683.37**	**5107.75**	**4757.19**	84	4087.599

BIC = Bayesian information criterion; AIC = Akaike information criterion; CAIC = consistent AIC; SABIC = sample size−adjusted BIC.
Bold indicates best-fitting model by each model fit index.

Appendix V
Model Fit Indexes for One- to Five-State Solutions of Received Life-Sustaining Treatments

State Number	Log Likelihood (LL)	BIC (LL)	AIC (LL)	CAIC (LL)	SABIC (LL)	Number of Parameters	Degrees of Freedom
1	−862.76	1761.68	1737.51	1767.68	1742.64	6	483.0782
2	−668.29	1414.94	1362.57	1427.94	1373.69	13	94.1418
3	−639.37	**1399.31**	1318.75	**1419.31**	1335.85	20	36.3153
4	−628.14	1419.05	**1310.29**	1446.05	**1333.37**	27	13.8552
5	**−625.51**	1455.98	1319.02	1489.98	1348.09	34	8.5824

BIC = Bayesian information criterion; AIC = Akaike information criterion; CAIC = consistent AIC; SABIC = sample size−adjusted BIC.
Bold indicates best-fitting model by each model fit index.
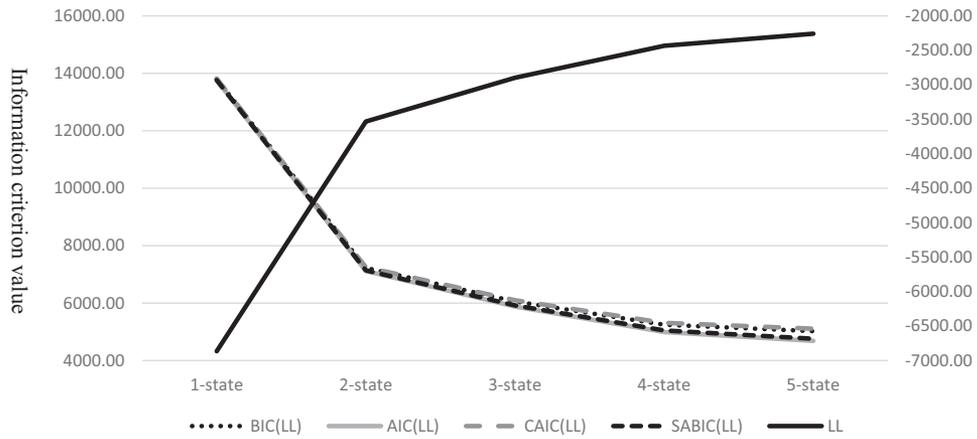
Appendix VI. Plots of AIC, BIC, CAIC, and SABIC values for preferred life-sustaining treatments. AIC = Akaike information criterion; BIC = Bayesian information criterion; CAIC = consistent AIC; SABIC = sample size−adjusted BIC.
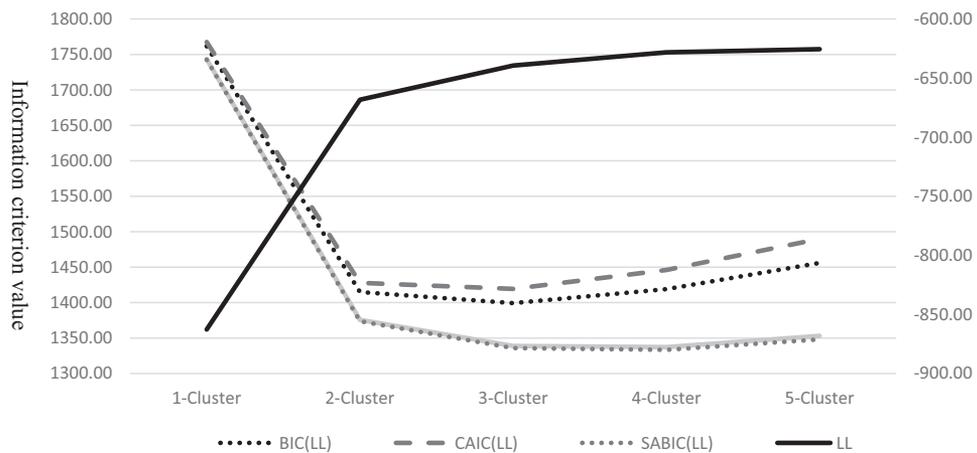
Appendix VII. Plots of AIC, BIC, CAIC, and SABIC values for received life-sustaining treatments. AIC = Akaike information criterion; BIC = Bayesian information criterion; CAIC = consistent AIC; SABIC = sample size−adjusted BIC.

Appendix VIII

**Transition Probabilities for States of Preferences for
Life-Sustaining Treatments From Time [t−1] to Time [t]
(*N* = 367)**

Time [t−1]	Time [t]		
State	1	2	3
1	**0.967**	0.020	0.014
2	0.005	**0.995**	0.001
3	0.027	0.006	**0.957**

Bold indicates the highest transition probability between different times. Among 425 participants, 58 were excluded from estimates of transition probabilities because they were only assessed once.