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Effect of Default Options in Advance Directives on Hospital-Free Days and Care Choices Among Seriously Ill Patients:

A Randomized Clinical Trial

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Abstract

IMPORTANCE—There is limited evidence regarding how patients make choices in advance directives (ADs) or whether these choices influence subsequent care.

OBJECTIVE—To examine whether default options in ADs influence care choices and clinical outcomes.

DESIGN, SETTING, AND PARTICIPANTS—This randomized clinical trial included 515 patients who met criteria for having serious illness and agreed to participate. Patients were enrolled at 20 outpatient clinics affiliated with the University of Pennsylvania Health System and the University of Pittsburgh Medical Center from February 2014 to April 2016 and had a median follow-up of 18 months. Data analysis was conducted from November 2018 to April 2019.

INTERVENTIONS—Patients were randomly assigned to complete 1 of the 3 following ADs: (1) a comfort-promoting plan of care and nonreceipt of potentially life-sustaining therapies were selected by default (comfort AD), (2) a life-extending plan of care and receipt of potentially life-sustaining therapies were selected by default (life-extending AD), or (3) no choices were preselected (standard AD).

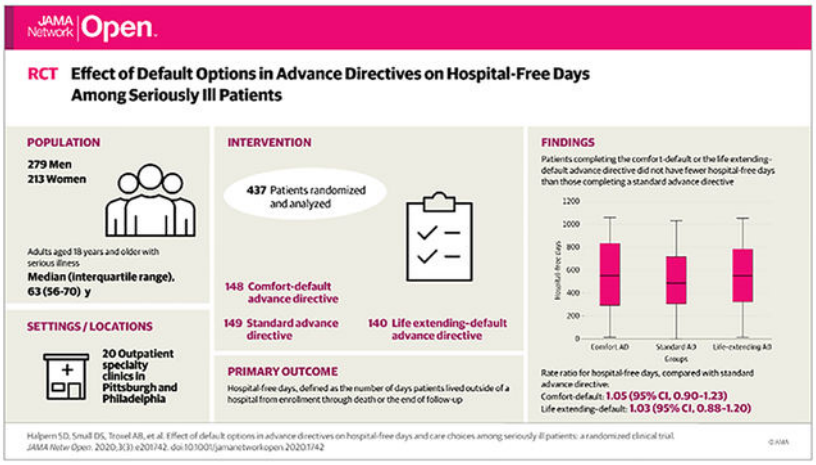
MAIN OUTCOMES AND MEASURES—This trial was powered to rule out a reduction in hospital-free days in the intervention groups. Secondary outcomes included choices in ADs for an overall comfort-oriented approach to care, choices to forgo 4 forms of life support, patients' quality of life, decision conflict, place of death, admissions to hospitals and intensive care units, and costs of inpatient care.

RESULTS—Among 515 patients randomized, 10 withdrew consent and 13 were later found to be ineligible, leaving 492 (95.5%) in the modified intention-to-treat (mITT) sample (median [interquartile range] age, 63 [56–70] years; 279 [56.7%] men; 122 [24.8%] black; 363 [73.8%] with cancer). Of these, 264 (53.7%) returned legally valid ADs and were debriefed about their assigned intervention. Among these, patients completing comfort ADs were more likely to choose comfort care (54 of 85 [63.5%]) than those returning standard ADs (45 of 91 [49.5%]) or life-extending ADs (33 of 88 [37.5%]) ($P = .001$). Among 492 patients in the mITT sample, 57 of 168 patients [33.9%] who completed the comfort AD, 47 of 165 patients [28.5%] who completed the standard AD, and 35 of 159 patients [22.0%] who completed the life-extending AD chose comfort care ($P = .02$), with patients not returning ADs coded as not selecting comfort care. In mITT analyses, median (interquartile range) hospital-free days among 168 patients assigned to comfort ADs and 159 patients assigned to life-extending default ADs were each noninferior to those among 165 patients assigned to standard ADs (standard AD: 486 [306–717] days; comfort AD: 554 [296–833] days; rate ratio, 1.05; 95% CI, 0.90–1.23; $P < .001$; life-extending AD: 550 [325–783] days; rate ratio, 1.03; 95% CI, 0.88–1.20; $P < .001$). There were no differences among groups in other secondary outcomes.

CONCLUSIONS AND RELEVANCE—In this randomized clinical trial, default options in ADs altered the choices seriously ill patients made regarding their future care without changing clinical outcomes.

TRIAL REGISTRATION—ClinicalTrials.gov Identifier: NCT02017548

Graphical Abstract



Effect of Default Options in Advance Directives on Hospital-Free Days Among Seriously Ill Patients

Introduction

Seriously ill patients are often hospitalized and receive life-sustaining therapies by default, ie, unless patients or their caregivers have specifically requested otherwise.[1,2] Advance directives (ADs) were created to enable the many patients who wish to forgo such aggressive care near the end of life[3,4] to set limits on their future therapies.[5] However, despite national policies and practices that increasingly encourage AD completion,[6–10] evidence regarding the benefits of AD completion, or of making certain choices within ADs, is limited.

The 2 randomized clinical trials[11,12] (RCTs) showing benefits of ADs included only very elderly patients who were already in nursing homes or hospitals. Observational studies have shown that patients who complete ADs in the community less commonly die in a hospital,[13–16] more often receive care consistent with their preferences,[15] and, in certain regions, receive less costly care.[16] However, the likelihood of unmeasured differences between patients who do and do not choose to complete ADs precludes inferences regarding whether AD completion or the choices made in ADs cause such benefits.[17,18]

Given the logistical and ethical difficulties of randomly assigning patients to complete ADs, we sought to determine whether the choices made in ADs could be altered using default options[19] and, if so, whether these experimentally induced differences in choices caused different patient outcomes. In a pilot RCT,[20] we randomly assigned 132 patients with advanced thoracic illnesses to complete 3 versions of real ADs with default options set to nudge certain treatment choices. These default options significantly influenced the treatments patients selected in the ADs without altering their satisfaction with advance care planning.[20] In the present trial, we sought to determine whether default options similarly influenced the AD choices made by a new and larger population of patients with a more

diverse range of chronic serious illnesses. We then tested the hypotheses that assignment to complete ADs with default options for overall care and for receiving 4 forms of life support would not reduce the primary outcome of days alive and outside of a hospital (ie, hospital-free days) and would improve secondary patient-reported and clinical outcomes. Finally, we sought to prospectively examine how often seriously ill patients make changes in legally valid ADs.

Methods

Trial Design

We conducted a 3-group RCT comparing patients who were encouraged to complete a standard AD or 1 of 2 ADs with different default options for overall goals of care and preferences to receive 4 forms of life support (ie, cardiopulmonary resuscitation, mechanical ventilation, dialysis, and a surgical feeding tube). The study protocol and statistical analysis plan have been described previously (Supplement 1)[21] and were approved by the institutional review boards at the University of Pennsylvania, the University of Pittsburgh, and Rowan University. This study followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline.

Study Population

Eligible patients were aged 18 years and older with 1 of the serious illnesses summarized in Table 1. They were recruited from 20 specialty clinics affiliated with the University of Pennsylvania Health System and the University of Pittsburgh Medical Center. *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* (*ICD-10*) codes were used to identify serious illnesses, and the limited exclusion criteria we applied have been described previously.[21]

From February 6, 2014, to April 15, 2016, recruiters screened electronic health records (EHRs) to identify eligible patients scheduled for outpatient visits the following week. When patients screened eligible, we notified the outpatient physician by email that we would recruit the patient at the next visit unless the physician requested otherwise by reply email. In the clinics, 1 of 6 recruiters approached each preliminarily eligible patient, described the rationale for AD completion, and sought patients' written consent to participate in a study comparing 3 different versions of legally valid ADs.[21] All consenting patients were given 1 of 3 randomly assigned AD versions, an informational brochure about ADs, the recruiter's contact information, and a stamped envelope addressed to study staff for returning the AD.

Recruiters encouraged patients to complete their ADs at home with their caregivers and/or with physicians and to return completed ADs, with the signatures of 2 witnesses or a notary, within 10 days. If a returned AD was not received within 10 days, research staff called patients weekly for up to 1 month to answer questions and remind patients to return their ADs (eFigure 1 in Supplement 2).

Randomization and Interventions

Patients were randomized individually to receive 1 of 3 versions of the AD with equal probabilities using electronic random number generation. Randomization was stratified by the 6 research coordinators who recruited patients from different clinics, and we used variable block sizes of 3 and 6 within each recruiter to promote balance. Each AD version was based on the professionally endorsed AD published by the Allegheny County Medical Society and aligned with Pennsylvania statutory guidance. We added 1 question to each AD version asking patients to choose an overall plan of care focused on life extension or comfort if those 2 goals were to come into conflict. Language from the Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments (SUPPORT) trial was used for this question.[22,23]

The differences in the 3 AD versions are described in eTable 1 in Supplement 2. In the standard AD, patients were asked to actively choose an overall goal of care and whether to receive each of 4 forms of life support. The comfort AD was identical to the life-extending AD, except the comfort plan of care (as opposed to the life-extension plan of care) was listed first and preselected, as were choices to forgo rather than receive the 4 life-sustaining interventions. Patients were informed by research staff and written instructions that other choices could be made by crossing out the preselected options and selecting alternatives, which were identical to those in the standard AD. Patients receiving standard ADs were secondarily randomized to receive a version with either comfort or life-extending options listed first. Because this was merely intended to mitigate ordering effects, all patients in the standard AD group were analyzed together. Thus, there were 3 groups with a total of 4 versions of the AD (eAppendix in Supplement 2).

Debriefing and Processing of ADs

Patients who returned ADs were called by a research coordinator who debriefed them about the precise differences between their assigned AD version and the versions received by other patients. Using an institutional review board–approved debriefing script also employed in our pilot study,[20] the coordinator ensured that patients understood the use of default options in the 3 AD versions. The coordinator then reviewed each choice the patient made and encouraged patients to make any changes to these choices before considering the AD complete. We then asked clinic staff to scan the completed ADs into the patient EHR and mailed completed versions to the patient, any identified surrogate, and other requested caregivers.

Outcomes

The primary outcome was hospital-free days, defined as the number of days patients lived outside of a hospital from enrollment through death or the end of follow-up on December 31, 2016. Research staff masked to the patients' assigned groups attempted to contact patients 2, 6, and 12 months after AD completion to assess secondary, patient-reported outcomes and to help patients make desired changes to their ADs. Decision conflict[24] was assessed immediately after patients completed their ADs. Satisfaction with advance care planning, measured with a global satisfaction question,[25,26] was assessed as close as possible to 2 months after AD completion. Quality of life was measured using the McGill

Quality of Life instrument[27,28] as close as possible to 6 months after AD completion. Other secondary outcomes included the choices patients made in their original ADs and choices to modify their AD selections during follow-up.

We used state databases capturing all admissions and inpatient procedures in Pennsylvania and New Jersey to measure survival, hospital and intensive care unit admissions, inpatient costs of care, and receipt of the previously described forms of life support. We had planned to measure surrogates' perceptions of the quality of death, bereavement outcomes, and health system distrust.[21] However, we abandoned this plan after roughly 100 patients were enrolled because of difficulties reaching surrogates within 3 months of patients' deaths. Owing to delays in obtaining finalized data from the state registries, the data set was considered final in November 2018, and analyses were conducted from November 2018 to April 2019.

Statistical Analysis

We used negative binomial regression to compare the number of hospital-free days among groups, and we used logistic, linear, negative binomial, or Cox proportional hazards models, as appropriate based on outcome parameterizations and distributions, for all secondary outcomes. In all analyses, we first modeled the patient's recruiter as a fixed effect to adjust for potential clustering. However, because recruiters worked in specific clinics, patient diagnosis and recruiter were collinear. Therefore, we calculated models with recruiter or with diagnosis (ie, cancer vs other) and report the latter because the coefficients for the intervention variables were nearly identical (Statistical Analysis Plan in Supplement 1).

Primary analyses of clinical outcomes were conducted in a modified intention-to-treat (mITT) sample, including all patients who were randomized, were not subsequently found to be ineligible, and did not withdraw consent. Analyses of patient-reported outcomes were conducted among patients who completed ADs and were debriefed. Choices made in ADs were analyzed in both groups. In the mITT sample, patients not completing ADs were considered to have not chosen comfort-oriented approaches to care and to have not chosen to forgo life support, consistent with the underlying defaults in clinical practice. We also evaluated how making certain choices in ADs affected hospital-free days using complier average treatment effect analyses,[29,30] which use the randomization ground as an instrumental variable to account for the AD noncompletion that we anticipated in advance.[21]

We decided a priori that if default options connoted harm, they would be unlikely to be used in ADs outside of research, even if they produced other benefits. Thus, although we were motivated to learn whether changing choices in ADs could improve a variety of patient-centered outcomes and used traditional superiority tests to compare these outcomes among arms, we sought to enroll enough patients to rule out, using noninferiority tests, the possibility that assignment to either of the default ADs would reduce patients' hospital-free days.[21] Specifically, we sought to rule out a rate ratio of less than 0.85, which corresponds to a 15% reduction in hospital-free days associated with use of a default AD compared with the standard AD. Simulations that conservatively assumed substantial data dispersion showed that enrolling 270 patients who completed ADs would enable a noninferiority test with 80%

power at this prespecified margin, accounting for the 2 primary hypothesis tests using a Bonferroni correction.

Data analysis was conducted using R version 3.4.2 (R Project for Statistical Computing) and Stata version 15 (StataCorp). Statistical significance was set at $P < .05$. The noninferiority tests were 1-tailed, and all other tests were 2-tailed.

Results

Among 917 patients who were eligible to participate and were approached, 515 (56.2%) consented and were randomized (Figure 1). Of these, 10 patients withdrew their consent and 13 were determined to be ineligible shortly after randomization, leaving 492 patients in the mITT sample. These patients had a median (interquartile range [IQR]) age of 63 (56–70) years, with 279 (56.7%) men, 122 (24.8%) black participants, 175 participants (35.6%) with a high school education or less, and 363 participants (73.8%) with an advanced cancer as their primary illness (Table 1).

Of these 492 patients, 14 (2.8%) did not survive for 30 days, 284 (59.4%) of the remaining 478 patients completed ADs, and 264 (93.0%) of these were successfully debriefed (median [IQR] 14 [5–35] days after returning the AD). The 264 patients who completed ADs and were debriefed were similar to the other 228 patients across all measured variables (eTable 2 in Supplement 2). The proportions of patients who completed ADs and were debriefed were similar across groups (Figure 1). Advance directives were scanned into the EHR for 186 of 264 patients (70.5%) a median (IQR) of 20 (9–47) days after debriefing. Final ADs were mailed to all patients and identified surrogates within a week of debriefing.

Choices Made in AD

Among the 264 patients who completed ADs and were debriefed, only 1 (0.4%) changed the choice they made regarding overall goals of care during debriefing and 10 or fewer (≤3.8%) changed their preferences regarding whether or not to forgo each form of life support (eTable 3 in Supplement 2). After incorporating these changes into the final ADs, patients completing comfort ADs were more likely to choose a comfort-oriented plan of care (54 of 85 [63.5%]) than patients completing standard ADs (45 of 91 [49.5%]) or life-extending ADs (33 of 88 [37.5%]) ($P = .001$) (Figure 2). This pattern was preserved among all 492 patients in the mITT sample after coding patients who had not returned ADs as having not chosen a comfort-oriented plan of care (comfort AD: 57 of 168 [33.9%]; standard AD: 47 of 165 [28.5%]; life-extending AD: 35 of 159 [22.0%]; $P = .02$) (Figure 2).

Similarly, in the per-protocol analysis, patients completing comfort ADs were more likely than patients completing other ADs to make choices to forgo mechanical ventilation (comfort AD: 47 [55.3%]; standard AD: 34 [37.4%]; life-extending AD: 34 [38.6%]; $P = .03$), dialysis (comfort AD: 46 [54.1%]; standard AD: 25 [27.5%]; life-extending AD: 29 [33.0%]; $P = .004$), and feeding tube insertion (comfort AD: 42 [49.4%]; standard AD: 34 [37.4%]; life-extending AD: 28 [31.8%]; $P = .02$), without corresponding differences for cardiopulmonary resuscitation (comfort AD: 27 [31.8%]; standard AD: 22 [24.2%]; life-extending AD: 19 [21.6%]; $P = .13$) (eFigure 2 in Supplement 2). In the mITT sample,

similar patterns were observed, but the difference was only statistically significant for forgoing dialysis (comfort AD: 49 [29.2%]; standard AD: 28 [17.0%]; life-extending AD: 32 [20.1%]; $P = .046$) (eFigure 3 in Supplement 2).

Clinical Outcomes

Of 492 patients in the mITT sample, 55 (11.2%) failed to provide valid social security numbers (SSNs), precluding linkages necessary to measure utilization outcomes. The 55 patients who did not provide valid SSNs were evenly distributed among the 3 groups (eTable 4 in Supplement 2). Compared with patients who returned valid SSNs, these patients were better educated (college and postcollege degree: 162 [37.1%] vs 31 [56.4%]; $P = .02$) and reported higher incomes (≥$100 000: 75 [17.2%] vs 21 [38.2%]; $P = .003$) but were otherwise similar (eTable 4 in Supplement 2). Median (IQR) follow-up for the 437 patients with valid SSNs was 18 (11–27) months.

The median (IQR) hospital-free days observed among patients assigned to the comfort AD and to the life-extending AD were not less than the median (IQR) number of hospital-free days among patients assigned to the standard AD (standard AD: 486 [306–717] days; comfort AD: 554 [296–833] days; rate ratio, 1.05; 95% CI, 0.90–1.23; $P < .001$; life-extending AD: 550 [325–783] days; rate ratio, 1.03; 95% CI, 0.88–1.20; $P < .001$) (Figure 3; eTable 5 in Supplement 2). A sensitivity analysis, in which hospital-free days were generated using multiple imputation for the 55 patients who did not provide valid SSNs produced similar results (eTable 6 in Supplement 2). Additionally, complier average treatment effect analyses revealed that choices to promote comfort care did not alter the number of hospital-free days (eTable 7 in Supplement 2).

In mITT analyses, the assigned AD version was not significantly associated with survival, hospital or intensive care admissions, place of death, receipt of any form of life support during follow-up, or costs of inpatient care (Table 2; eTable 8 and eTable 9 in Supplement 2). Because these analyses may be biased toward the null by including all randomized and eligible patients, we performed a post hoc analysis limited to the 179 patients who completed ADs, were debriefed, had their ADs uploaded into the EHR, and provided a valid SSN. These patients were equally represented among the 3 trial groups (eTable 10 in Supplement 2). In this restricted sample, patterns of choices made in the 3 AD versions were similar to those observed among all patients completing ADs (eTable 11 in Supplement 2), and there remained no significant associations of AD version with hospital-free days, days in the hospital, or receipt of any life-sustaining therapy (eTable 11 in Supplement 2).

Patient-Reported Outcomes

Among patients who completed ADs, the version they were assigned to complete was not associated with their levels of decision conflict or satisfaction with advance care planning (Table 2). Quality of life was reported by 247 patients and imputed for the remaining 17 patients. Median (IQR) quality of life scores were 8.34 (5.80–8.97), 8.43 (7.00–8.92), and 7.67 (6.28–8.48) among patients who completed the comfort AD, standard AD, and life-extension AD, respectively (adjusted P values among groups were all >.20) (eTable 12 in Supplement 2).

Discussion

In this RCT of different types of legally valid ADs, we found that default options strongly influenced the choices that seriously ill patients made regarding their overall goals of care and often their expressed preferences to receive life support. Despite this effect on patients' choices, default options in ADs did not reduce the primary outcome of hospital-free days nor did they yield improvements in any secondary patient outcomes.

The effects of default options on patients' choices for their future care were observed despite only considering choices final after we described the defaults to patients and reassessed their choices. Thus, these results are unlikely to be due to inattention or misunderstanding and are instead consistent with how defaults have been shown to be interpreted as recommendations and thereby influence many clinical and nonclinical decisions.[19,31–37] Choices regarding end-of-life care are conventionally thought to reflect personal and deep-seated values. The present RCT, coupled with the parallel results from our prior RCT among a smaller and less diverse sample of patients,[20] challenges this standard view. Further challenging this view are data from a 2019 RCT,[38] in which encouraging seriously ill patients to deliberate on their preferences for end-of-life care did not yield choices that differed from those made by patients who were forced to choose quickly and intuitively. Together, these results support the view that, for many seriously ill patients, end-of-life care choices do not stem from patients' underlying values but rather are constructed, at least in part, during the process of elicitation.[1,39,40]

This RCT confirmed our hypothesis that, despite encouraging more seriously ill patients to choose comfort-oriented goals of care and to forgo forms of life support, comfort-oriented default options would not reduce these patients' hospital-free days. However, contrary to our hypotheses, the use of default options did not meaningfully change any secondary clinical or patient-reported outcomes. Specifically, in the full sample, no differences were found for quality of life, satisfaction with advance care planning, decisional conflict, survival, place of death, hospitalizations, intensive care unit admissions, or costs of inpatient care. Similarly, in the sample restricted to patients who completed all elements of the protocol, no differences among groups were identified in any of the analyzed outcomes. Although this study was not specifically powered to identify differences in these outcomes, the consistency of the results suggests limits to the benefits of conventional ADs as deployed in general practice.

This RCT also provides prospective evidence that seriously ill patients rarely choose to modify their ADs, even when actively prompted to do so. This supports and extends prior work using retrospective designs or hypothetical ADs that also found preferences to be largely stable over time.[23]

Limitations

This study has limitations. First, we were unable to obtain sufficient measures of quality of life among patients who did not return ADs to conduct a prespecified[21] complier average treatment effect analysis assessing the effect of choosing comfort care on this outcome. Second, due to low rates of caregiver response to our bereavement assessments following patients' deaths, we could not achieve our goal of examining how AD defaults affected

caregiver outcomes.[21] Third, due to limitations in the administrative data, we could not reliably measure hospice use or duration of hospice use before death.

Fourth, despite frequently encouraging patients to complete the ADs that were given to them, more than 40% of enrolled patients did not do so. Despite frequently asking clinic staff to upload completed ADs to the EHR, nearly 30% of such ADs were not uploaded. These limitations in AD completion and accessibility as well as the relatively low rates of hospitalization and life-sustaining therapy use in this sample could have biased the RCT to confirming noninferiority on the primary outcome and contributed to the null effects observed among secondary outcomes. However, the observations that the randomly assigned AD version significantly influenced choices without altering any outcomes among the restricted sample with full protocol adherence provides confidence that these results were not spurious. Furthermore, although default options altered patients' choices in the mITT and per-protocol samples, complier average treatment effect analyses that accounted for protocol nonadherence provided no evidence that these altered choices led to differences in hospital-free days. These observed limitations in intended care processes reflect the reality of current policies and practices regarding the completion of ADs outside of research. In fact, the rates of AD completion and EHR accessibility observed in this trial were greater than the corresponding rates observed in clinical settings.[41–43]

Conclusions

This RCT showed that the choices made by many seriously ill patients in legally valid ADs are influenced by how options are framed, suggesting that such patients' preferences do not stem solely from deeply held values or goals. Although helping seriously ill patients endorse limitations on the aggressiveness of their future care did not worsen any outcomes measured, the absence of clear benefits precludes a recommendation that default options be routinely implemented in ADs. Rather, the observation that randomly assigned default options influenced choices without changing outcomes suggests that current policies and practices that encourage the completion of conventional ADs[6–10] may not improve the quality of end-of-life care.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Key Points

Question

What effects do default options on advance directives have on the choices made by seriously ill patients and their future outcomes?

Findings

In this randomized clinical trial of 492 seriously ill patients, default options in advance directives strongly influenced patients' goals of care and preferences for receiving life support, even though patients were told of these defaults. Advance directives with defaults did not reduce the primary outcome of hospital-free days during a median follow-up of 18 months compared with advance directives without defaults, nor did they improve other patient-reported, clinical, or economic outcomes.

Meaning

The findings of this study suggest that seriously ill patients' end-of-life care choices are strongly influenced by the way choices are framed, but changing choices in conventional advance directives is unlikely to change patient outcomes.

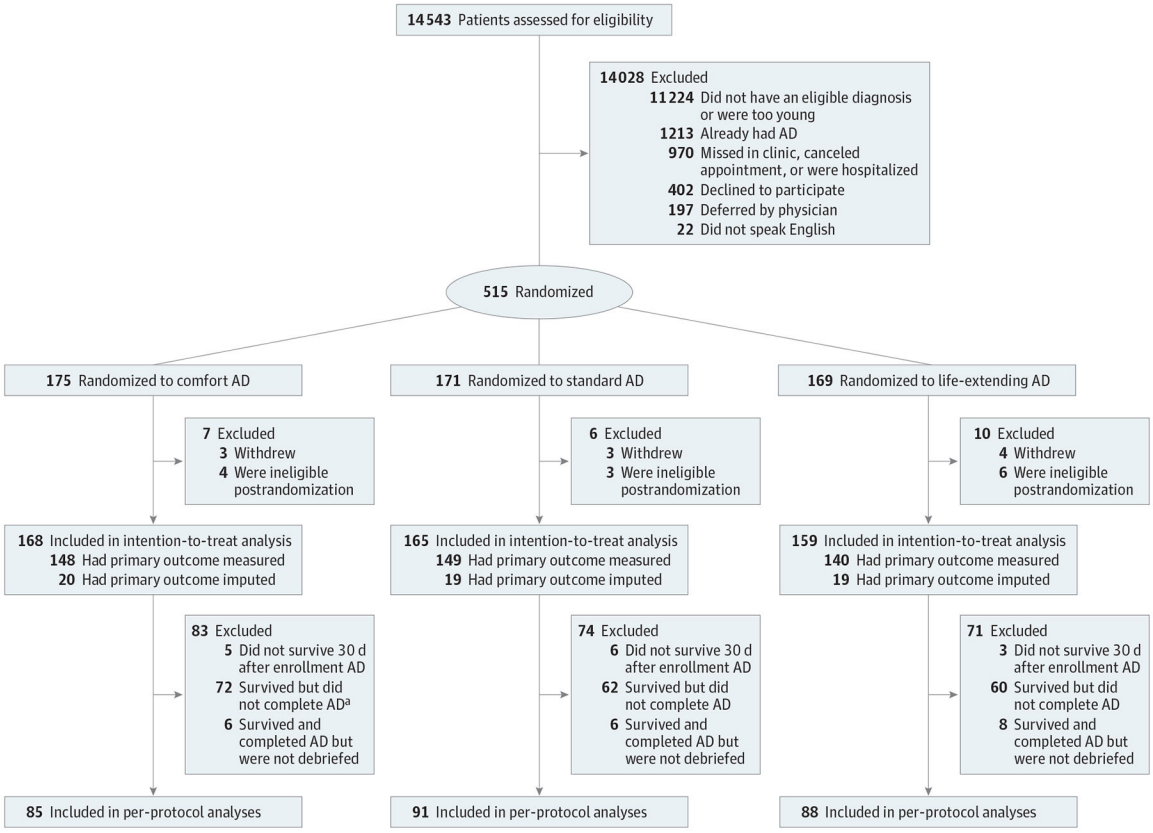

Figure 1. Patient FlowDiagram

AD indicates advance directive.

[a] *P* for AD completion and debriefing by treatment group = .62

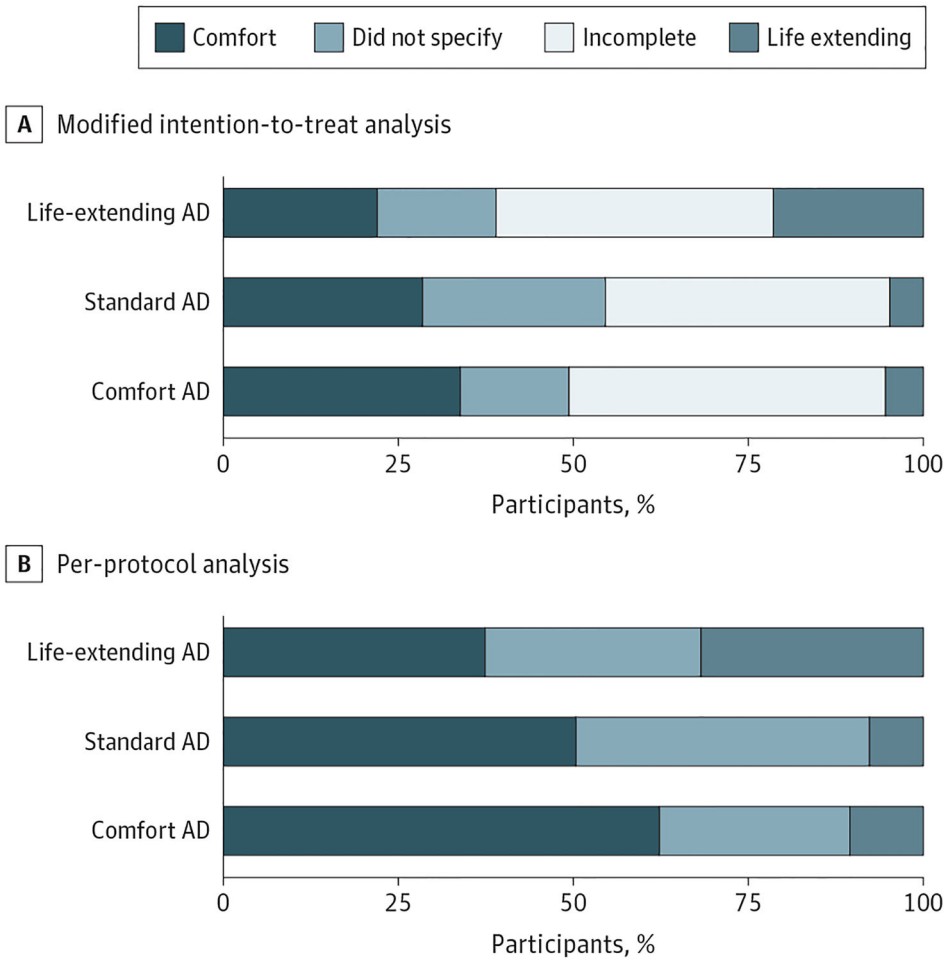

Figure 2. Selected Goals of Care Chosen

A, The first panel plots the proportions of the 492 patients in the modified intention-to-treat analysis who chose comfort-oriented care, life-extending care, and choices not to specify a preference. The 228 patients who did not complete an advance directive (AD) and/or were not debriefed are coded as incomplete. B, The second panel plots the same proportions among the 264 patients with completed ADs who were also debriefed.

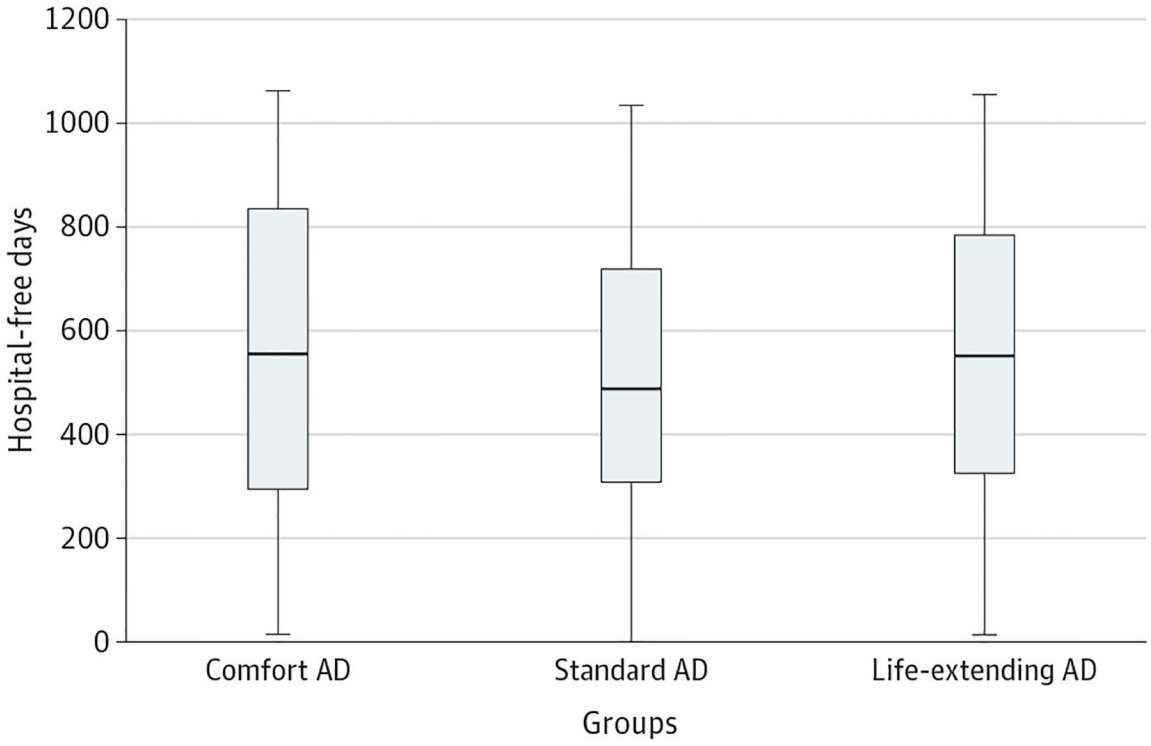

Figure 3. Hospital-Free Days

This figure plots hospital-free days among the 492 patients in the modified intention-to-treat sample across the 3 intervention arms. The horizontal line represents the median; the height of the box, the interquartile range; and the vertical lines, the range.

Table 1.

Characteristics of the 492 Participants in the Modified Intention-to-Treat Sample

	No. (%)		
Characteristic	**Comfort AD (n = 168)**	**Standard AD (n = 165)**	**Life-extending AD (n = 159)**
Age, mean (SD), y	62.16 (11.65)	62.93 (9.79)	61.92 (11.45)
Sex			
Men	102 (60.7)	88 (53.3)	89 (56.0)
Women	66 (39.3)	77 (46.7)	70 (44.0)
Race			
White	116 (69.0)	115 (69.7)	116 (73.0)
Black or African American	45 (26.8)	42 (25.5)	35 (22.0)
Other	6 (3.6)	7 (4.2)	7 (4.4)
Missing or unknown	1 (0.6)	1 (0.6)	1 (0.6)
Ethnicity			
Not Hispanic or Latino	143 (85.1)	142 (86.1)	142 (89.3)
Hispanic or Latino	4 (2.4)	2 (1.2)	2 (1.3)
Missing or unknown	21 (12.5)	21 (12.7)	15 (9.4)
Marital status			
Currently married or living with partner	99 (58.9)	107 (64.8)	109 (68.6)
Divorced or separated	26 (15.5)	25 (15.2)	22 (13.8)
Never married	30 (17.9)	21 (12.7)	17 (10.7)
Widowed	13 (7.7)	8 (4.8)	10 (6.3)
Missing	0	4 (2.4)	1 (0.6)
Education			
<High school	8 (4.8)	10 (6.1)	7 (4.4)
High school or GED	48 (28.6)	54 (32.7)	48 (30.2)
Some college	40 (23.8)	33 (20.0)	44 (27.7)
College degree	37 (22.0)	41 (24.8)	37 (23.3)
>College	32 (19.0)	24 (14.5)	22 (13.8)
Missing	3 (1.8)	3 (1.8)	1 (0.6)
Income, $			
<30 000	53 (31.5)	37 (22.4)	38 (23.9)
30 000–69 999	57 (33.9)	60 (36.4)	57 (35.8)
70 000–99 999	22 (13.1)	25 (15.2)	24 (15.1)
≥100 000	32 (19.0)	32 (19.4)	32 (20.1)
Missing	4 (2.4)	11 (6.7)	8 (5.0)
Religion			
Catholic	58 (34.5)	49 (29.7)	65 (40.9)
Protestant	62 (36.9)	60 (36.4)	53 (33.3)
Other Christian	19 (11.3)	21 (12.7)	8 (5.0)

	No. (%)		
Characteristic	**Comfort AD (n = 168)**	**Standard AD (n = 165)**	**Life-extending AD (n = 159)**
Jewish	7 (4.2)	8 (4.8)	4 (2.5)
Other faiths	4 (2.4)	6 (3.6)	6 (3.8)
Unaffiliated	13 (7.7)	15 (9.1)	17 (10.7)
Missing	5 (3.0)	6 (3.6)	6 (3.8)
Diagnosis			
Cancer	121 (72.0)	127 (77.0)	115 (72.3)
COPD and other incurable lung disease	19 (11.3)	15 (9.1)	11 (6.9)
End-stage renal disease	11 (6.5)	9 (5.5)	14 (8.8)
Congestive heart failure	4 (2.4)	4 (2.4)	3 (1.9)
Amyotrophic lateral sclerosis	13 (7.7)	10 (6.1)	16 (10.1)

Abbreviation: AD, advance directive; COPD, chronic obstructive pulmonary disease; GED, general education diploma.

Table 2.

Summary of Adjusted Comparisons of Secondary Outcomes Across Groups

Outcome	Raw score[a]			Estimation method	Adjusted effect estimate (95% CI)		Comfort AD vs standard		Life-extending AD vs standard	
	Comfort AD	Standard AD, reference	Life-extending AD		Comfort AD	Life-extending AD	Unadjusted *P* value[b]	Adjusted *P* value	Unadjusted *P* value[b]	Adjusted *P* value
Decision conflict total score, mean (SD)[c]	17 (12.4)	16.2 (13.8)	17.4 (13.9)	Linear change from reference	0.51 (−3.83 to 4.85)	1.5 (−2.91 to 5.9)	.73	.82	.60	.50
Very satisfied with advance care planning, No./total No. (%)[d]	68/71 (95.8)	69/76 (90.8)	62/69 (89.8)	Odds ratio	2.31 (0.60 to 11.17)	0.95 (0.30 to 2.97)	.24	.25	.85	.93
McGill Quality of Life, mean (SD)[e]	6.2 (3.2)	6.4 (3.2)	5.9 (3.1)	Linear change from reference	0.11 (−0.85 to 1.07)	−0.04 (−0.99 to 0.92)	.82	.82	.38	.94
Survival, median (iQR), d[f]	564 (302.8 to 843.2)	494 (717 to 316)	553.5 (325.8 to 791.2)	Hazard ratio	0.66 (0.37 to 1.19)	0.83 (0.45 to 1.51)	.04	.17	.39	.54
Died in hospital, No./ Total No. (%)[g]	13/148 (8.8)	23/149 (15.4)	14/140 (10)	Odds ratio	0.52 (0.24 to 1.05)	0.61 (0.29 to 1.23)	.08	.08	.15	.17
Hospital admissions, median (IQR), No.[h]	1 (0 to 2)	1 (0 to 3)	1 (0 to 2)	Incident rate ratio	0.98 (0.72 to 1.33)	0.87 (0.63 to 1.18)	.57	.88	.24	.37
ICU admissions, median (IQR), No.[h]	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	Incident rate ratio	0.91 (0.46 to 1.81)	0.84 (0.4 to 1.73)	.72	.79	.61	.64
Total cost of inpatient care, median (IQR), thousands of $[i]	28.7 (0 to 188.1)	60.7 (0 to 267.8)	31.9 (0 to 162.2)	Log linear change from reference	−1.09 (−2.43 to 0.25)	−0.78 (−2.14 to 0.58)	.11	.11	.22	.26
Cost of inpatient care per hospitalization day, median (IQR), thousands of $[i]	6.7 (0 to 3.2)	9.4 (0 to 15.0)	7.1 (0 to 16.0)	Log linear change from reference	−0.9 (−1.97 to 0.16)	−0.52 (−1.6 to 0.56)	.09	.97	.30	.35
Receipt of life-sustaining therapy, No./ Total No. (%)[j]	16/148 (10.8)	20/149 (13.4)	15/140 (10.7)	Odds ratio	0.64 (0.3 to 1.33)	0.72 (0.34 to 1.51)	.49	.48	.24	.39

Abbreviations: AD, advance directive; ICU, intensive care unit; IQR, interquartile range.

[a]The number of responses is different for different outcomes, given that patient-reported outcomes were collected only for per-protocol sample and there are some missing responses.

[b] Unadjusted *P* values are reported from univariate analysis. The adjustments include patient characteristics such as age, gender, race, and education.

[c] The estimate for patients' decision conflict scale is the ordinary least square estimate. A total of 71 patients in the comfort AD group, 75 patients in the standard AD group, and 68 patients in the life-extending AD group completed this measure.

[d] Satisfaction scale analyzed as binary variable with levels very satisfied and not very satisfied. The data used in the model were responses of the patients after approximately 2 months of AD completion.

[e] McGill Quality of Life is reported for 247 patients and imputed for 17 patients, for a total of 264 patients (85 in the comfort AD group, 91 in the standard AD group, and 88 in the life-extending AD group). The regression table and imputation method are described in eTable 12 in Supplement 2. The reported estimate is the mean response from linear regression model. Among these 247 scores, 3 are calculated from a surrogate's response

[f] Survival data were available for all participants. Survival was analyzed using Cox proportional hazards model.

[g] Place of death categorized as death at the hospital and other. The other category includes death at other places and patients who were still alive.

[h] Hospital admissions and ICU admissions are treated as counts, and suitable count models have been used to model those outcomes. The reported estimates are incident rates. Hospital admission data were available for all participants. For ICU admissions, data were available only from Pennsylvania database, representing 143 patients in the comfort AD group, 134 patients in the standard AD group, and 124 patients in the life-extending AD group.

[i] Total cost of inpatient care and cost of inpatient care per day were available for all participants. The cost analysis was done by log transforming inpatient care charges. The reported estimates are βs. The decrease of hospital-free days in the intervention arm = $(e^{X}(\beta)-1) \times 100\%$.

[j] Percentage of patients receiving any 1 of cardiopulmonary resuscitation, mechanical ventilation, dialysis, or surgical feeding tube.