Original Article

Advance Directives, Medical Conditions, and Preferences for End-of-Life Care Among Physicians: 12-year Follow-Up of the Johns Hopkins Precursors Study

Joseph J. Gallo, MD, MPH, Martha Abshire, PhD, RN, Seungyoung Hwang, MS, MSE, and
Marie T. Nolan, PhD, RN
Johns Hopkins University Bloomberg School of Public Health (J.J.G., S.H.), Baltimore, Maryland; Johns Hopkins University School of Nursing (M.A., M.T.N.), Baltimore, Maryland; and American Psychiatric Association (S.H.), Washington, D.C., USA

Abstract

Context. Stability of preferences for life-sustaining treatment may vary depending on personal characteristics.

Objective. We estimated the stability of preferences for end-of-life treatment over 12 years and whether advance directives and medical conditions were associated with change in preferences for end-of-life treatment.

Design. Mailed survey of older physicians.

Methods. Longitudinal cohort study of medical students in the graduating classes from 1948 to 1964 at Johns Hopkins University. Eight hundred ninety eight physicians who completed the life-sustaining treatment questionnaire anytime in 1999, 2002, 2005, and 2011 (mean age 68.2 years at baseline). Preferences for life-sustaining treatment were assessed using a checklist questionnaire in response to a standard "brain injury" scenario and considered as a package using the latent class transition model.

Results. End-of-life preferences grouped into three classes: most aggressive (wanting most interventions; 14% of physicians), least aggressive (declining most interventions; 61%), and an intermediate class (declining most interventions except intravenous fluids and antibiotics; 25%). Physicians without an advance directive were more likely to desire more treatment and were less likely to transition out the most aggressive class. Transition probabilities from class to class did not vary over time. Persons with cancer expressed preference for the least aggressive treatment, whereas persons with cardiovascular disease and depression had preferences for more aggressive treatment.

Conclusion. Transitions in end-of-life preferences and the factors influencing change and stability suggest that periodic reassessment for planning end-of-life care is needed. J Pain Symptom Manage 2019;57:556–565. © *2018 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.*

Key Words
End-of-life preferences, latent transition analysis, advance directives

Introduction

Despite the emphasis on achieving good-quality end-of-life care by documenting preferences, factors related to eliciting end-of-life preferences, such as stability of choices, have not been extensively studied in community-dwelling older adults. Progress has been made in palliative care, including new interventions to improve patient outcomes[1–4] and increased availability of palliative care services at hospitals with more than 50 beds,[5] but health services research

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Address correspondence to: Joseph J. Gallo, MD, MPH, Department of Mental Health, Bloomberg School of Public Health, Johns Hopkins University, 624 North Broadway, Baltimore, MD 21205, USA. E-mail: jgallo2@jhu.edu

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shows that care in the last months of life is not improving. Between 2000 and 2009, days in the intensive care unit, transitions in care,[6] and cancer chemotherapy near death became more common,[7] and the trends are worsening.[6] One in eight family members reported care in the last month of life was inconsistent with patient wishes.[8] Our study of physicians' preferences for their own end-of-life care encompasses a life course, longitudinal perspective. As participants in the cohort have aged, end-of-life preferences for treatments have become personally salient.

Although studies of preferences for end-of-life care over the last two decades have extended our knowledge of factors involved in change of preferences, studies are marked by limitations, including small sample size (e.g., 150 or fewer[9–12]) and a wide range of time intervals between preference assessments (e.g., less than one month[13] to one year or more[10,14–17]). Few studies have assessed change of preferences over a span of time greater than two years.[18,19] Most studies are restricted only to persons whose life expectancy was limited or unknown or focus on wishes for only one or two interventions (e.g., cardiopulmonary resuscitation[20,21]). The full spectrum of life-sustaining interventions beyond resuscitation to include intravenous hydration, chemotherapy, invasive testing, and other treatments is rarely studied. Few studies have examined the treatment preferences of community-dwelling adults and even fewer have captured the preferences of a large sample repeatedly over an extended period of time at ages when end-of-life decision-making becomes more salient with increasing presence of medical conditions.

Despite the considerable advantages of longitudinal studies over cross-sectional designs, the interpretation of change in life-sustaining treatment preferences may be difficult because, for most samples, the understanding of medical treatments may be highly variable. Persons with limited knowledge of medical interventions may construct their preferences "on the spot" or imagine health states based on personal knowledge, the experiences of family or friends, or through media depictions, which may be quite different than likely outcomes.[22] Our study capitalizes on a decades-long follow-up of physicians who have participated since they were medical students at Johns Hopkins between 1946 and 1964. Physicians require little explanation about a given clinical situation, nor to understand potentially life-sustaining treatments. Because physicians understand serious illness, treatment, and prognosis,[23] by studying them we sharpen the focus on factors that might influence how preferences change over time while minimizing changes due to shifting knowledge about disease and treatment.

Our strategy was to ask participants to consider what types of treatment they would want if they suffered irreversible brain damage that left them unable to speak understandably or to recognize people.[18,20,24] We selected the scenario of irreversible brain damage without terminal illness because previous research demonstrated that this scenario provided a greater degree of variability of responses than other vignettes in the medical directive.[25,26] The use of a scenario 1) provides a common stimulus to gauge preferences for end-of-life care across a large sample and over time; 2) is a signal for whether the respondent would want to be treated aggressively given an ambiguous clinical situation; 3) describes a common clinical situation at the end of life similar to the end stages of Alzheimer's disease or cancer; and 4) can be evaluated in the context of a longitudinal study with information on behaviors specifically related to end-of-life planning.

We had two related aims. First, we wanted to describe change in preferences over a 12-year period. Because we assessed preferences every 3 years over the 12-year follow-up in the same cohort, we could evaluate whether transitions from more aggressive to less aggressive preferences, or *vice versa*, change as the cohort ages. The extended follow-up allows us to examine if transitions become more marked as the cohort ages because we are studying the same people at different ages (not different people at different ages as in most studies that examine age differences in preferences). Second, we modeled the relationship between certain chronic medical conditions and transitions of preferences for end-of-life treatment and considered the presence of an advance directive. We hypothesized that the presence of certain chronic medical conditions (cardiovascular disease [CVD], diabetes, cancer, and depression) or having an advance directive would be associated with transitions to less aggressive preferences for treatment at the end of life.[18,27,28] The overarching goal was to contribute to our understanding of the factors associated with preferences for end-of-life care and how they change over the course of an extended 12-year follow-up.

Methods

The Johns Hopkins Precursors Study

The Johns Hopkins Precursors Study began in 1946 as a prospective longitudinal study that enrolled graduating classes of 1948 to 1964 of the Johns Hopkins School of Medicine.[29] Over 6000 variables were collected at baseline, and annual follow-up has been conducted since graduation. Since the initial evaluation in medical school, questionnaires have been mailed annually to detect incident disease, risk factors, and health behaviors. Since 1988, there has been increased use of standardized questionnaires. We follow up participants who do not respond to the annual questionnaire with intensive follow-up activities (e.g., postcards, telephone calls) and resend the questionnaire if necessary. The content of the questionnaires has changed over time to be consistent with aging of the sample (e.g., inclusion of assessment of functional impairment) and varies somewhat from year to year, based on the need for periodic reassessments and the interests of faculty and students (e.g., assessing functional impairment every 2—3 years; addition of questionnaires on resilience and planning for future incapacity). Precursors Study procedures are reviewed by the Johns Hopkins University School of Medicine Institutional Review Board annually.

Assessment of Preferences for Potentially Life-Sustaining Treatment

The 1999, 2002, 2005, and 2011 questionnaires asked participants to consider what types of treatment they would want if they suffered irreversible brain damage that left them unable to speak understandably or to recognize people.[25,26] In the scenario, the participants were told that they had no terminal illness and might remain in this brain-injured state for a long period of time.[25,26] These conditions were selected to reflect a common scenario at the end of life among those with advanced chronic illness; physical impairment accompanied by diminished cognitive capacity until death. Participants were asked to state their wishes regarding the use of 10 medical interventions: CPR, mechanical ventilation, intravenous fluids, surgically placed feeding tube for nutrition, dialysis, chemotherapy, major surgery, invasive diagnostic tests, blood or blood products, and antibiotics. Responses for each intervention were coded a priori into a dichotomous variable as either *reject* (“no, I would not want”) or *accept* (yes, undecided, or trial of treatment). This dichotomization reflects common clinical practice in which “treatment trial” and “unsure” would translate into providing life-sustaining treatment to incompetent patients, at least initially.[18]

Covariates

Taken together, the four conditions selected (CVD, diabetes, cancer, and depression) have high public health significance and were selected to provide a guide as to how use of advance directives and transitions might vary in common chronic conditions. Self-reports of medical conditions by physicians are highly accurate, as assessed by comparison of reported conditions on questionnaire to in-person physical examination.[29] Presence of medical conditions was based on lifetime self-report. Depression was assessed with the Patient Health Questionnaire-9 (a threshold of 10 and above was taken as evidence of depression[30,31]). Physicians were asked to indicate whether they had established any form of advance directive for themselves.[24]

Analytic Strategy

Our analysis proceeded in two phases. First, to study potentially life-sustaining treatments as a class or set of treatments (“latent status”) in contrast to a focus on individual interventions, we applied the latent transition model.[32,33] The model provides for simultaneous estimation of 1) latent status membership probabilities in 1999; 2) transition probabilities from one class of preferences to another over time; and 3) item-response probabilities conditional on latent status membership and time. Persons who had preference data at only one time point contributed to estimates of preference class but not to transition probability. Missing data and attrition on latent status indicators are permitted and taken into account when parameters are estimated by maximum likelihood using the expectation-maximization algorithm within the latent transition analysis procedure.[34] Statistical analyses were performed using Mplus version 7.1 and PROC LTA in SAS version 9.4. Model choice, in terms of the number of latent classes, was determined through examination of fit indices, model identification (e.g., homogeneity and latent class separation), and clinically interpretable results. Bayesian Information Criteria (BIC[35]) were used to compare non-nested models that differed in the number of latent classes. A smaller value of BIC indicates a better model fit. The four-class model yielded the best fit over two- or three-class models using statistical criteria ($BIC_2 = 18{,}973.73$; $BIC_3 = 17{,}465.72$; $BIC_4 = 17{,}353.06$). However, the more parsimonious model was chosen because of good latent class separation with the latent classes appearing conceptually distinct overall.[32,36]

Second, medical conditions (i.e., CVD, diabetes, cancer, and depression) and presence of an advance directive were separately added to the three-status model as a grouping variable to examine the extent to which the latent status prevalence at Wave 1999 and transition probabilities were the same or different across two groups (defined by the presence or absence of each medical condition or advance directive). Using the robust maximum likelihood estimator, comparison between the two nested models was tested through the likelihood-ratio test under measurement invariance across both groups and times.[32,37] Results were considered statistically significant if the two-sided p-value was less than 0.05.

Results

Sample Characteristics

In total, 1337 participants were eligible for participation, but 338 persons died before 1999 (the first year for which preferences were assessed), leaving 999 persons. Among them, we excluded 101 persons because of incomplete information on preferences for the brain injury scenario for all four waves. We used all 898 participants (456 had all four waves of end-of-life preferences data; 204 had three; 115 had two; 123 had one). In 102 cases, there was no 1999 data on preferences, but they still contributed to the estimates for the overall model. In all, 796 responded to the brain injury scenario with expressions of treatment preferences in 1999, 744 in 2002, 681 in 2005, and 568 in 2011. The mean age ± standard deviation of the study sample at baseline was 68.2 ± 5.4 years. Reflecting medical school enrollment between 1948 and 1964, the study sample was 92% white men. We found that 392 (44%), 304 (34%), and 123 (14%) had lifetime chronic CVD, cancer, and diabetes, respectively. In all, 227 (25%) participants had depression and 741 (83%) had a living will or durable power of attorney for health care.

Structure of Treatment Preference Categories Over Time

Latent class transition analysis demonstrated that end-of-life preferences for treatments in the case of irreversible brain damage grouped together in three groups in 1999 and similarly in 2002, 2005, and 2011 (discussed in detail by Wittink et al.[18]): 1) one class was characterized by participants who wanted most interventions ("most aggressive" category); 2) the second class was characterized by participants who declined most interventions ("least aggressive"

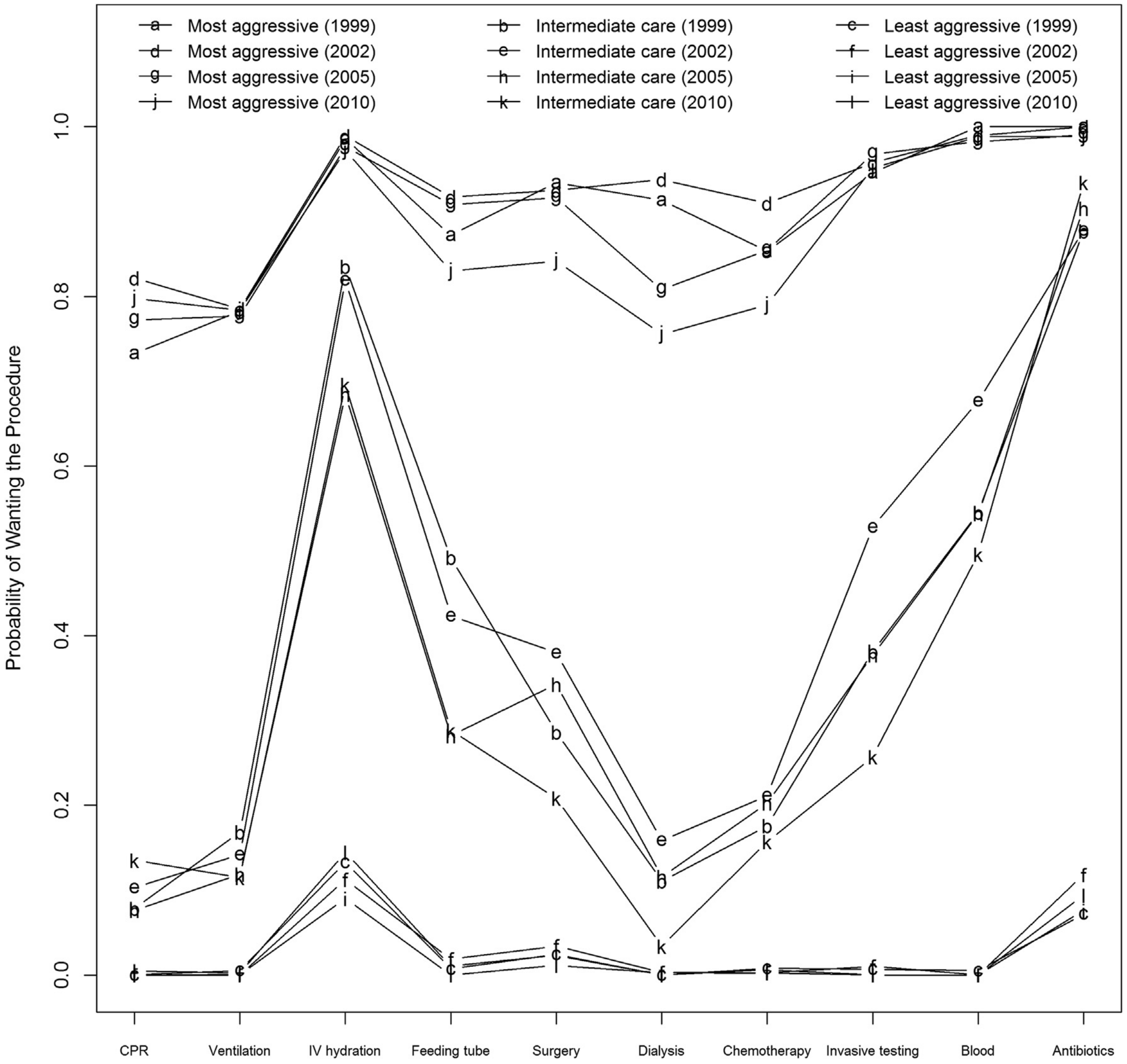

Fig. 1. Probability of desiring specific interventions given class of desire for aggressiveness of care. Data are from The Johns Hopkins Precursors Study (1999–2011).

category); and 3) an intermediate class ("intermediate care") in which the primary interventions desired were intravenous fluids and antibiotics. Of note, when considering the prioritization of various treatments given aggressive treatment category, participants in all three groups were more likely to consider intravenous fluids and antibiotics than other treatments.

The vertical axis in Figure 1 shows the probability of desiring specific interventions among persons in a given category of treatment preferences (most aggressive, least aggressive, and intermediate care categories). The similar structure of the item-response parameters across time suggested that the interpretation of the three latent classes was consistent over time. Based on the hypothesis test of measurement invariance across times, parameter restrictions were imposed so that the item response probabilities were equal across time intervals.

Preferences and Advance Directives

Overall, 14% of physicians were in the most aggressive class at Wave 1999, 25% were in the intermediate class, and 61% were in the least aggressive class. Figure 2 shows significant differences in prevalence of advance directives in preferences for end-of-life care in 1999 (the likelihood-ratio statistic $G^2 = 170.84$ with df = 2, $P < 0.001$), with physicians without living will or durable power of attorney for health care more likely to belong to the most aggressive class than those with an advance directive (25% vs. 12%), and less likely to belong to the least aggressive class (47% vs. 64%).

Transition probabilities between assessment intervals were not significantly different from one interval to another; therefore, we imposed parameter restrictions so that the transition matrices for each group were equal across the four time intervals. Transition probabilities are thus presented as *time i* to *time i+1*. In other words, the transition probabilities from one preference category to another were the same whether the time interval was 1999 to 2002, 2002 to 2005, or 2005 to 2011 (implying no change in the nature of transitions with age). Inspection of the diagonal elements of the transition probability matrices in Table 1 shows that the respondents with an advance directive were more likely to transition out of the most aggressive class than were respondents without an advance directive (0.50 vs. 0.64), likewise for the intermediate class (0.51 vs. 0.71); so having an advance directive was associated with transitions to less aggressive care preferences.

Preferences and Chronic Medical Conditions

No statistically significant differences in latent status prevalence were observed between respondents with specific medical conditions and those who never had the condition (all $P > 0.05$; Fig. 3). Nevertheless, persons with cancer tended to have a higher prevalence of preference for the least aggressive treatment, whereas persons with CVD and depression tended to have a higher prevalence of preference for the most aggressive treatment. Persons with CVD or diabetes, compared with persons without the conditions, tended to be more stable in the most aggressive category and less stable in the least aggressive category (Table 2).

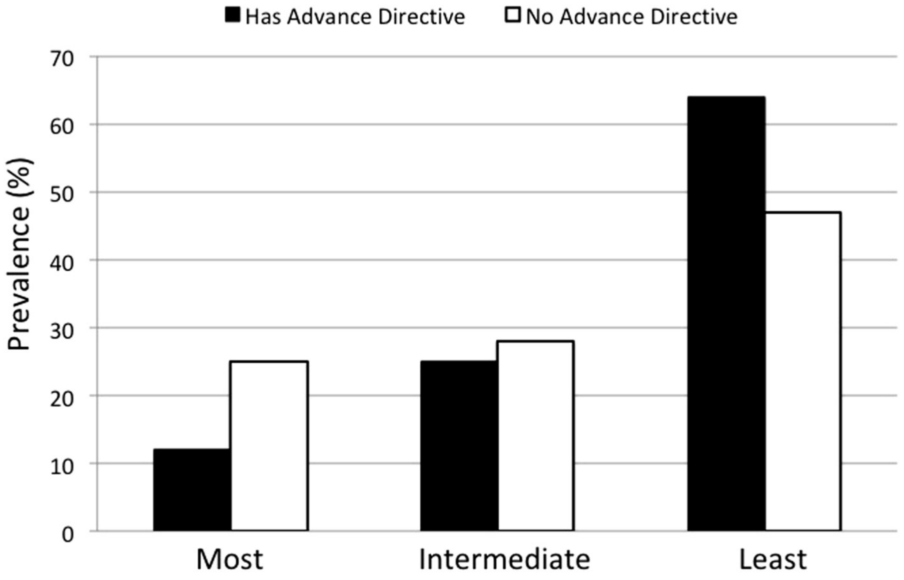

Fig. 2. Initial preferences of aggressiveness of care according to whether the participant had an advance directive.* Data are from The Johns Hopkins Precursors Study (1999–2011). * $P < 0.001$ ($G^2 = 170.84$ with df = 2).

Table 1
Probability of Having a Preference for Most Aggressive, Intermediate Care, or Least Aggressive End-of-Life Care at *time i+1* Given Preference at *time i*, According to Whether the Participant Has an Advance Directive

	time i+1		
time i	Most Aggressive	Intermediate Care	Least Aggressive
Has advance directive			
Most aggressive	0.50	0.30	0.20
Intermediate care	0.16	0.51	0.32
Least aggressive	0.06	0.14	0.80
No advance directive			
Most aggressive	0.64	0.09	0.27
Intermediate care	0.19	0.71	0.10
Least aggressive	0.13	0.14	0.73

Data are from the Johns Hopkins Precursors Study (1999−2011).
$P < 0.001$ ($G^2 = 146.94$ with df = 6).

Discussion

Addressing the quality of care at the end of life in the U.S., the Institute of Medicine Report *Dying in America* emphasized the role of advance care planning for improving end-of-life care.[38] The *Summit on the Science of Compassion* sponsored by the National Institute of Nursing Research described an urgent need for studies that go beyond a single-disease cross-sectional approach to examine end-of-life issues in longitudinal studies of established cohort.[39] Our cohort study of physicians elicited preferences for 10 specific treatments given a brain injury scenario, classifying participants into most aggressive, intermediate, and least aggressive categories based on the responses. We designed this study with the assumption that assessment of categories of aggressiveness is more clinically relevant than methods that evaluate the difference in the number of interventions accepted[28,40,41] or assess only acceptance or rejection of CPR.[12,27] Participants without a living will or durable power of attorney for health care were more likely to belong to the most aggressive class than those with advance directives, and less likely to belong to the least aggressive class. Estimates of the prevalence of each category of aggressiveness for end-of-life treatment revealed that persons with CVD and depression had the highest prevalence for aggressive treatment. Persons with cancer had the highest prevalence of persons preferring the least aggressive treatment. Participants with an advance directive were more likely to transition out of the most aggressive category than were respondents without an advance directive. Persons with CVD or diabetes, compared with persons without the conditions, tended to be more stable in the most aggressive category and less stable in the least aggressive category.

Before discussing the implications of our study, we need to consider potential limitations of our study. First, the study cohort consisted of mostly older white, male physicians who graduated from the same medical school and participated in a longitudinal study. Studies have revealed higher rates of advance directive completion among whites compared with minority older adults.[42] Second, respondents may have made transitions in the three-year intervals between assessments that were unobserved. In addition, losses due to death increase with age mean that transitions among older groups may be more likely to be unobserved. Third, by eliciting treatment preferences using a hypothetical illness scenario, preferences might not accurately predict treatment decisions during actual illness. Because of space constraints in the questionnaire, we were only able to use one scenario to elicit preferences. Fourth, we examined the association between diagnoses of medical conditions and not perceived quality of life or illness experiences that might have been more salient for older adults. We could not examine diabetes complications separately, nor did we have a large enough sample to study changes in medical conditions. Finally, although the latent transition model is a powerful statistical method for making sense of preference data over time, we were limited in being able to examine potential interactions between medical conditions and presence of advance directives. We are carrying out semistructured interviews with physicians and family members to understand what factors are most important from the perspective of physicians and family members themselves.

Persons who had issued an advance directive were less likely to belong to the most aggressive class of care than those who did not issue an advance directive. Persons with an advance directive who were in the most aggressive class were likely to transition to a less aggressive class over time. This finding is consistent with the findings of the systematic review by Auriemma et al. (2014) who found that those who issued an advance directive were more likely to express preferences to forgo life-sustaining therapies and that those who chose to forgo therapies demonstrated greater stability over a one-year time period than those who preferred to receive life-sustaining therapies.[43] In addition, intravenous fluids and antibiotics seemed to be viewed differently across aggressive preference categories. Perhaps this is because in contrast to chemotherapy, antibiotics are viewed as a treatment that can have a relatively immediate positive effect if there is going to be a positive effect at all and IV is the delivery method required in a patient too sick to take oral medications. Further study should explore why antibiotics were

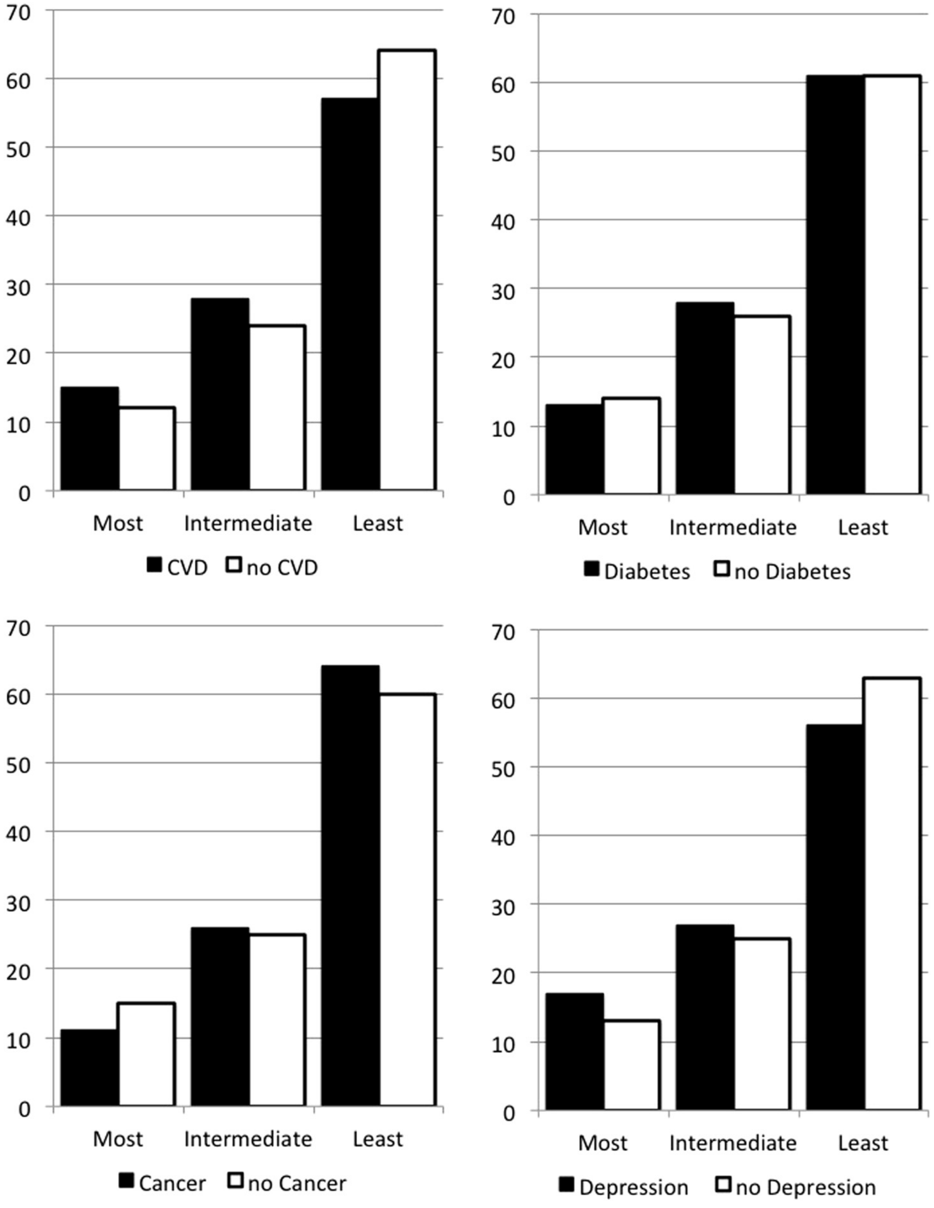

Fig. 3. Initial preferences of aggressiveness of care according to whether the participant has cardiovascular disease (CVD), diabetes, cancer, or depression (black bars) or not (white bars).* Data are from The Johns Hopkins Precursors Study (1999–2011). * $P > 0.05$ for all comparisons.

preferred by those in the different aggressive treatment preference categories. More than 80% had a documented advanced directive or living will, which far exceeds the 51%, 18%, and 15% obtained by whites, Hispanics, and blacks, respectively, in a U.S. nationally representative sample.[42] Advance directives appear to be written to signify what one *does not* want rather than what one *does* want at the end of life. Nevertheless, among participants with an advance directive, 20% of the persons who preferred the least aggressive treatment changed over time. This challenges the practice of not incorporating end-of-life preference conversations if an advanced directive is already documented. The circumstances under which such transitions are made require attention in cohort studies exploring the how and why of individual decision-making.

Persons with cancer had the highest prevalence of preference for the least aggressive treatment (64%), which likely reflects a better understanding of the illness trajectory among patients with cancer than those with other conditions.[44] A systematic review of 59 studies found that persons with serious illness were more likely to forgo life-sustaining treatments than those without serious illness.[43] Estimates of the prevalence of each category of aggressiveness for

Table 2

Probability of Having a Preference for Most Aggressive, Intermediate Care, or Least Aggressive End-of-Life Care at *time i+1* Given Preference at *time i*, According to Whether the Participant Has a Cardiovascular Disease, Diabetes, Cancer, or Depression

	Present			Not Present		
	time i+1			*time i+1*		
time i	Most Aggressive	Intermediate Care	Least Aggressive	Most Aggressive	Intermediate Care	Least Aggressive
Cardiovascular disease, $P = 0.02$ ($G^2 = 14.86$ with df = 6)						
Most aggressive	0.55	0.26	0.19	0.52	0.26	0.22
Intermediate care	0.18	0.56	0.26	0.15	0.52	0.33
Least aggressive	0.07	0.18	0.75	0.06	0.12	0.83
Diabetes, $P = 0.006$ ($G^2 = 18.18$ with df = 6)						
Most aggressive	0.57	0.11	0.32	0.53	0.28	0.19
Intermediate care	0.23	0.49	0.28	0.16	0.54	0.30
Least aggressive	0.06	0.18	0.76	0.06	0.13	0.80
Cancer, $P = 0.44$ ($G^2 = 5.84$ with df = 6)						
Most aggressive	0.46	0.30	0.24	0.56	0.24	0.20
Intermediate care	0.21	0.52	0.27	0.14	0.54	0.31
Least aggressive	0.06	0.16	0.78	0.07	0.13	0.80
Depression, $P = 0.32$ ($G^2 = 7.06$ with df = 6)						
Most aggressive	0.54	0.28	0.18	0.53	0.25	0.22
Intermediate care	0.12	0.60	0.29	0.18	0.52	0.30
Least aggressive	0.09	0.14	0.77	0.06	0.14	0.80

Data are from the Johns Hopkins Precursors Study (1999–2011).

end-of-life treatment revealed that persons with CVD and depression had the highest prevalence of a category in which all most aggressive treatments were desired. In previous work with this cohort over a shorter follow-up time (6 years), we found that persons with declining function and depression were five times more likely to desire aggressive treatment than were respondents without functional decline or depression.[20] This is consistent with a study by Stevenson et al. (2008) that reported that persons with advanced heart failure whose symptoms improved with hospitalization were more likely to have increased preferences for survival after discharge.[45] As symptoms of chronic illness worsen, individuals with these conditions may desire less aggressive care. In contrast, a study of 265 lay persons with chronic pulmonary disease, congestive heart failure, and chronic renal failure for whom worsening symptoms of anxiety and depression increased the probability of changing from accepting CPR to refusing CPR at the end of life.[46] The Janssen study was considering use of CPR as a life-sustaining treatment, whereas aggressive treatment in our study could include IV hydration, chemotherapy, and invasive testing in addition to resuscitation.

Concerns about "generalizability" of the findings should be balanced with broad consensus of the need for longitudinal, prospective studies of preferences for care.[39,47] We argue that the findings are significant *because* the subjects are physicians. Although physicians may grasp the facts of their clinical situation more quickly and completely than the average patient (e.g., on prognosis with chemotherapy[48]), comprehension of the clinical situation does not necessarily translate into emotional understanding, easy adjustment to bad news, or adherence to preventive services or healthy habits.[49,50] Physician-patients and families are no less likely than others to experience difficulties, to have poor coping strategies, or to benefit from professional advice and help.[51–53] The impact and significance of our study is more than academic since the public has an interest in "how doctors die"[54]—why and how is it that doctors generally do not wish treatments they often recommend to patients? What physicians do for themselves in end-of-life planning and decisions is a bellwether for the leading edge of change and for narratives of changing preferences.

Disclosures and Acknowledgments

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