Stability of Preferences for End-of-Life Treatment After 3 Years of Follow-up

The Johns Hopkins Precursors Study

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Background: Preferences for life-sustaining treatment elicited in one state of health may not reflect preferences in another state of health.

Methods: We estimated the stability of preferences for end-of-life treatment across 3 years and whether declines in physical functioning and mental health were associated with changes in preferences for end-of-life treatment. In this longitudinal cohort study of medical students in the graduating classes of 1948 to 1964 at Johns Hopkins University, 818 physicians completed the life-sustaining treatment questionnaire in 1999 and 2002 (mean age at baseline, 69 years).

Results: Although the prevalence of the 3 clusters of life-sustaining treatment preferences remained stable across the 3-year follow-up, certain physicians changed their preferences with time. The probability that physicians were in the same cluster at follow-up as at baseline was 0.41 for “most aggressive,” 0.50 for “intermediate care,” and 0.80 for “least aggressive.” Physicians without advance directives were more likely to transition to the most aggressive cluster than to the least aggressive cluster during the 3-year follow-up (odds ratio, 1.96; 95% confidence interval, 1.11-3.45). Age at baseline and decline in physical and mental health were not associated with transitions between 1999 and 2002.

Conclusion: Periodic reassessment of preferences is most critical for patients who desire aggressive end-of-life care or who do not have advance directives.

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Crossing the Quality Chasm called for a vision of the health system that is more responsive to the wishes and preferences of patients. Nowhere is the quality of care more dependent on eliciting patient and family wishes and values than in the arena of end-of-life care. Quality end-of-life care, as outlined by Singer and colleagues,2 depends on eliciting the preferences of patients and families regarding the following goals: receiving adequate pain and symptom management, avoiding inappropriate prolongation of dying, achieving a sense of control, relieving the burden on loved ones, and strengthening relationships with loved ones. Nevertheless, various studies revealed that 4 in 10 dying patients had severe pain most of the time,3 almost half of incurably ill patients with advanced dementia and cancer received nonpalliative treatment,4 and bereaved family members believed that communication concerning end-of-life care issues was poor.5 Efforts to improve the experience of patients and families at the end of life must incorporate patient perspectives. Advance directives are 1 strategy through which patient preferences can be elicited and recorded, to be invoked at a time when the patient may not be able to make decisions directing care. Since advent of the Patient Self-Determination Act, hospitals, nursing homes, and health care programs have been required to ask patients about advance directives and to incorporate the information into medical records. Physicians are being encouraged to work with patients and families to complete advance directives in the outpatient setting. Despite the emphasis on eliciting and documenting preferences for good quality end-of-life care, to our knowledge, factors related to clinical aspects of eliciting end-of-life preferences, such as stability of choices, have not been extensively studied in community-dwelling older adults.

We estimated the stability of preferences for end-of-life treatment during 3 years and whether declines in physical functioning and mental health were associated with changes in preferences for end-
of-life treatment in participants in one of the oldest aging studies in the world, The Johns Hopkins Precursors Study. Given the age and functional status of the physician respondents, end-of-life considerations are a reality, not just hypothetical based on previous work6,7; we hypothesize that transitions to more aggressive categories of treatment preference might be more likely in respondents without advance directives or with declining self-rated physical function and mental health.

THE JOHNS HOPKINS PRECURSORS STUDY
The Johns Hopkins Precursors Study was designed in 1946 by Caroline Bedell Thomas to identify characteristics associated with premature cardiovascular disease and death.8-11 All 1337 students who matriculated into the graduating classes of 1948 to 1964 at The Johns Hopkins University School of Medicine were eligible. Precursors Study procedures have been reviewed and approved by The Johns Hopkins University School of Medicine institutional review board.

ASSESSMENT OF PREFERENCES FOR POTENTIALLY LIFE-SUSTAINING TREATMENT
The 1999 and 2002 questionnaires included items about whether the participating physician had or was considering obtaining a living will or durable power of attorney for health care. Participants were also asked to consider what types of treatment they would want if they experienced irreversible brain damage that left them unable to speak understandably or to recognize people.6,7 In the scenario, based on the medical directive developed by Emanuel and Emanuel,12 the participants were told that they had no terminal illness and might remain in this brain-injured state for a long time. We selected the scenario of irreversible brain damage without terminal illness because in previous research12,13 this scenario provided a greater degree of variability of responses than did other vignettes in the medical directive. The participants were asked to state their wishes regarding the use of 10 medical interventions: cardiopulmonary resuscitation, mechanical ventilation, intravenous fluids, surgically placed feeding tube for nutrition, dialysis, chemotherapy, major surgery, invasive diagnostic tests, blood or blood products, and antibiotics.8 The 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 has been used by other investigators and reflects common clinical practice in which “treatment trial” and “unsure” would translate into providing life-sustaining treatment to incompetent patients, at least initially.6,7,14

ASSESSMENT OF PHYSICAL FUNCTIONING AND MENTAL HEALTH
The 36-Item Short Form Health Survey (SF-36) was administered to the Precursors Study cohort as part of the annual questionnaires in 1999 and 2002 and was scored using standard techniques.15 The SF-36 has been used in studies of patient care outcomes16-20 and is reliable and valid in older adults.21-23 The mental health subscale, known as the 5-item version of the Mental Health Inventory, has been found to be an accurate screening instrument for the detection of major depression and other affective disorders.24 Because there are no standardized thresholds for dichotomized change scores on the SF-36 subscales, thresholds for significant changes in physical functioning and depression were established a priori based on clinically significant thresholds reported in a psychometric analysis of the SF-36.25 The physical functioning change score was dichotomized at 20 (ie, a decline of ≥20 points on the physical functioning subscale between the 1992 and 1998 questionnaires represented a clinically meaningful decline in physical functioning) and the depression change score at 5.

ANALYTIC STRATEGY
To study potentially life-sustaining treatments as a pattern or set of treatments (“latent classes”) in contrast to a focus on individual interventions, we applied the latent transition model.6,26 This model provides for simultaneous estimation of (1) clusters of end-of-life treatment preferences, (2) transition probabilities from one cluster of preferences to another, and (3) predictors of transitions from one cluster to another. We discuss the details of the latent transition model in the eFigure (http://www.archinternmed.com).

Data analysis was performed using Mplus version 4.1 and WinLTA version 3.1, which both use an efficient estimation-maximization algorithm for maximum likelihood estimation.26 Model choice, in terms of the number of latent classes, was determined through examination of fit indices and in relation to clinically interpretable results. Bayesian information criteria (BIC)26 were used to compare nonnested models that differed in the number of latent classes. A smaller value of BIC indicates a better model fit. A goodness-of-fit statistic, $G^2$, was used to assess the model goodness of fit for nested models with the same number of latent classes but that differed in the number of factors estimated.31 The 3-class model yielded the best fit at both time points over 2- and 4-class models using statistical criteria (BIC$_3=9262.64$, BIC$_4=9477.47$, and BIC$_{2}=10046.22$).

RESULTS

SAMPLE CHARACTERISTICS
The effective sample size for this analysis was 818 physicians. Of the 1016 participants to whom questionnaires were sent in 1999, 773 responded with their preferences for the brain injury scenario (76.1% participation). In 2002, 970 participants were sent questionnaires, and 721 were returned with information about end-of-life preferences (74.3% participation). Persons who had preference data at only 1 time point contributed to estimates of preference class and not to transition probability. The mean (SD) age of the study sample at baseline was 69.0 (5.4) years. Reflecting medical school enrollment between 1948 and 1964, the study sample was 92.0% white men. The mean (SD) physical functioning score as assessed using the SF-36 was 86.1 (20.3) in 1999 and 83.5 (20.9) in 2002. The mean (SD) mental functioning score as assessed using the SF-36 was 85.0 (11.8) in 1999 and 86.2 (10.4) in 2002.

CHANGE IN SPECIFIC INTERVENTION PREFERENCES BETWEEN 1999 AND 2002

Table 1 provides preferences for life-sustaining treatments in response to the hypothetical scenario in 2002 by preferences assessed in 1999. In general, procedures
that were declined in 1999 were likely also to be declined in 2002. Nevertheless, a substantial proportion of persons who desired an intervention in 1999 declined the treatment in 2002.

### TREATMENT PREFERENCE CATEGORIES IN 1999 AND 2002

Preferences derived from the latent transition model grouped together the same way in 1999 and in 2002: (1) a cluster representing desiring most interventions (“most aggressive” category), (2) a cluster declining most interventions (“least aggressive” category), and (3) an intermediate cluster (labeled “intermediate care”) in which the primary interventions desired were only intravenous fluids and antibiotics. The Figure shows the probability of desiring specific interventions given treatment preferences in 1999 and in 2002. The vertical axis in the Figure shows the probability of desiring specific interventions among persons in a given category of treatment preferences (most aggressive, least aggressive, and intermediate care categories).

### TRANSITIONS BETWEEN 1999 AND 2002

Although preferences for end-of-life care clustered together in the same way in 1999 and in 2002 (Figure), respondents moved from one cluster to another during the 3-year follow-up (Table 2). For example, among persons in the most aggressive category of preferences, the probability of remaining in the most aggressive category 3 years later was 0.41 (Table 2).

### COVARIATES AND TRANSITIONS BETWEEN 1999 AND 2002

The association of covariates with change in preference between 1999 and 2002, as measured using the odds ratio, is given in Table 3. Age and decline in mental or physical health (measured using the SF-36) were not statistically significantly associated with transitions to the most aggressive category compared with transitions to the least aggressive category (the associated confidence intervals included the null). However, physicians who reported having no living will or durable power of attorney were twice as likely to move to the most aggressive category as to the least aggressive category of potentially life-sustaining treatments (odds ratio, 1.96; 95% confidence interval, 1.11-3.45). Table 3 shows that there were no statistically significant associations of specific covariates with transition to the intermediate care category compared with transition to the least aggressive category.

### COMMENT

The latent transition analysis allowed us to classify preferences for end-of-life treatment into 3 clinically relevant clusters based on responses of physicians to a standard assessment instrument asking about 10 potentially...
Table 2. Probability of Being in a Specific Potentially Life-Sustaining Treatment Preference Category in 2002 Given Treatment Preferences in 1999

<table>
<thead>
<tr>
<th>Category of Treatment Preferences in 2002 (Estimated Prevalence)</th>
<th>Most Aggressive (14%)</th>
<th>Intermediate Care (26%)</th>
<th>Least Aggressive (60%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most aggressive (12%)</td>
<td>0.41</td>
<td>0.33</td>
<td>0.26</td>
</tr>
<tr>
<td>Intermediate care (26%)</td>
<td>0.20</td>
<td>0.50</td>
<td>0.30</td>
</tr>
<tr>
<td>Least aggressive (62%)</td>
<td>0.06</td>
<td>0.14</td>
<td>0.80</td>
</tr>
</tbody>
</table>

Data are from The Johns Hopkins Precursors Study (1999-2002).

Table 3. Association of Covariates With Transitions to the Most Aggressive Category vs the Least Aggressive Category and Transitions to Intermediate Care vs the Least Aggressive Category

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Transition to Most Aggressive Category vs Least Aggressive Category</th>
<th>Transition to Intermediate Care vs Least Aggressive Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥70 y in 1999 (reference: &lt;70 y)</td>
<td>0.93 (0.53-1.61)</td>
<td>1.05 (0.66-1.68)</td>
</tr>
<tr>
<td>Decline in mental health from 1999 to 2002 of ≥5 points (reference: &lt;5-point decline)</td>
<td>0.88 (0.46-1.69)</td>
<td>0.68 (0.37-1.24)</td>
</tr>
<tr>
<td>Decline in physical health from 1999 to 2002 of ≥20 points (reference: &lt;20-point decline)</td>
<td>0.95 (0.38-2.37)</td>
<td>0.86 (0.40-1.83)</td>
</tr>
<tr>
<td>No living will or durable power of attorney for health care (reference: having a living will or durable power of attorney for health care)</td>
<td>1.96 (1.11-3.45)</td>
<td>0.98 (0.58-1.67)</td>
</tr>
</tbody>
</table>

Odds Ratio (95% Confidence Interval)

Data are from The Johns Hopkins Precursors Study (1999-2002).

life-sustaining interventions. Although the preferences as tapped by the instrument seemed to cluster the same way in 1999 and in 2002 (most aggressive, least aggressive, and intermediate care), the likelihood that physicians changed their preferences for end-of-life care was related to their cluster at baseline. Most physicians in this sample fit into the least aggressive treatment preference category, and the physicians who chose least aggressive treatments at baseline were the least likely to change preferences with time (80% of persons in the least aggressive category at baseline were in the same category at follow-up). Physicians in the most aggressive category of preferences at baseline were the most likely to change preferences across time (41% of the persons in the most aggressive category at baseline were in the same category at follow-up). In addition, we found that physicians without advance directives were twice as likely as those with advance directives to transition to the most aggressive category compared with a transition to the least aggressive category during the 3-year follow-up. Age and decline in physical or mental health as measured using a standard instrument were not associated with transitions in preference categories.

Before discussing the implications of these findings, it is important to consider the potential limitations of this study. First, the study sample was a cohort of older physicians who graduated from a single medical school and have participated in a longitudinal study. The generalizability of the results may be limited to physicians. However, because older physicians are highly likely to have had professional experience with the life-sustaining treatments and the complications of severe irreversible brain damage as presented in the questionnaire, these results are unlikely to be affected by participant misunderstanding of the conditions and interventions asked about in the questionnaire. Also, we would argue that because the respondents are physicians, and previous studies suggest that experience with specific treatments may be associated with stability in preferences for health care, the estimates of change are likely to be conservative. In other words, we would expect this sample to provide an estimate of changeability that would be more stable than that of samples of persons with less medical education or experience. However, we acknowledge the possibility that physicians may have been influenced by answering the study questions or may have seen patient cases that changed their minds about their preferences. Second, the measures of physical and mental health were based on subjective assessment by the respondents and not on objective evaluation. Yet, the participants were physicians, who have been shown to provide accurate reports of their health. Third, we classified the respondents using a statistical model to characterize preferences. We believe that this categorization was more clinically relevant than methods that either evaluated the difference in the number of interventions accepted or assessed only acceptance or rejection of cardiopulmonary resuscitation. Fourth, we dichotomized the responses to the scenario so that those who were “unsure” or wanted “a treatment trial” were counted as desiring that treatment. Although this reflects common clinical practice in which “treatment trial” and “unsure” would translate into providing life-sustaining treatment to incompetent patients, we realize that this limits our ability to study transitions involving those responses. Fifth, by eliciting treatment preferences using a hypothetical illness scenario, the preferences we elicited might not accurately predict treatment decisions during actual illness. On the other hand, because hypothetical scenarios are frequently used in advance directive documents, our method reflects common medical practice regarding planning for end-of-life care. Finally, although these findings suggest that physicians without advance directives had less stable preferences across time than those with advance directives, we cannot rule out the possibility that persons who choose to have advance directives strongly desire less treatment at the end of life.

Prospective studies that have examined factors associated with change in preferences for end-of-life care have been limited to persons with severe physical illness, residents of nursing homes, and the recently hospital-
ized or have assessed preferences for single interventions only, such as cardiopulmonary resuscitation. Among severely ill patients (advanced cancer, congestive heart failure, or chronic obstructive pulmonary disease), results have been mixed. Persons with decline in physical functioning were more likely to accept treatment even if the outcome was predicted to be a diminished state of health. Subsequent study of the same cohort incorporated the trade-off of burden of treatment with potential outcomes of treatment. The proportion of persons who would undergo therapy with a given likelihood of death or disability were similar during follow-up, but individuals were less likely to want burdensome treatment across time. Greater functional disability and poor quality of life were associated with decreased willingness to undergo treatment. McParland and coworkers studied the preferences of nursing home residents for life-sustaining treatment for 2 years, finding no association between change in preferences and physical functioning. Carmel and Mutran interviewed (3 times in 2 years) a sample of 1138 persons 70 years and older living in the community in Israel. At each interval, approximately 70% of the sample did not change their preferences for aggressiveness of care, and the remainder was split between wanting more care and wanting less. Of persons who declined life-sustaining treatment at baseline, 87% continued to decline treatment 2 years later. Recognizing that negative findings are difficult to generalize, we did not find an association between change in mental or physical health (measured using the SF-36) and change in preferences for potentially life-sustaining treatment. Perhaps because physicians understand the course of disease and the nature of potentially life-sustaining treatments better, in this cohort, factors other than age, physical functioning, and mental health seem to play a role in transitions between categories of potentially life-sustaining treatments.

The treatment options offered at the end of life fell into preference categories that were clinically meaningful. The latent transition analysis sharpens the focus on the role of advanced directives aside from its association with preference category. Given that physicians without advance directives were more likely to change to the more aggressive category than to the least aggressive category with time, the process of documenting specific wishes may make decision making more deliberate, leading to more stability of preferences. Among physicians, advance directives seem to be used to signify what one does not want rather than what one does want at the end of life. Older adults focus on preferences for perceived outcomes of serious illness rather than in terms of preferences for specific treatment options. Refocusing advance directives on delineation of acceptable health states (ie, the outcomes of treatment) instead of preferences for specific medical interventions might better capture end-of-life care goals.

We believe that the results of this study suggest that although physician-respondents were relatively stable in their preferences, persons without advance directives and who desired the most aggressive treatment at baseline exhibited the most changeable preferences. We did not find evidence that changing mental or physical health was strongly associated with preferences for care. Persons who express a desire for aggressive treatment and those who have not communicated their wishes with a more formal written document (advance directives) may require frequent clinical reevaluation to assess whether wishes have changed. We are conducting open-ended interviews of respondents to understand the rationale for preferences for end-of-life care, to evaluate how and why preferences might change, and to determine whether the focus on potentially life-sustaining treatment in advance directives might be redirected to more salient domains, such as values or outcomes.

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Additional Information: The eFigure is available at http://www.archinternmed.com.

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The Latent Transition Model

The first part of the model groups interventions into clusters representing preferences for treatment. Let $U$ denote a response pattern of preferences for potentially life-sustaining treatments. The probability of a given pattern of preferences equals

$$Pr(U = u) = \sum_{k=1}^{K} P(C = k) P(U = u | C = k),$$

where $C$ denotes the latent class indicator (the latent status or category of the preferences for potentially life-sustaining treatment). We estimated $Pr(U = u | C = k)$ using logistic regression.

The second part of the model estimates transition probabilities among classes. The transition probability represents the probability that a respondent will desire a specific group of potentially life-sustaining treatments at follow-up given that they desired a specific set of treatments at baseline. A latent transitional model incorporated waves of data from 1999 and 2002 to study the stability of decisions across time. Let $Y = (Y_{11}, \ldots, Y_{1J}, Y_{21}, \ldots, Y_{2J})$ denote $J$ dichotomous variables, at both waves, indicating preference for a given intervention (e.g., cardiopulmonary resuscitation). For the transitional model with 2 time points, the probability of a response pattern across both periods equals

$$P(Y = y | x) = \sum_{c_1 = 1}^{S} \sum_{c_2 = 1}^{S} P(C_1 = c_1 | x) P(C_2 = c_2 | C_1 = c_1, x) \prod_{j=1}^{J} P(Y_{1j} = y_{1j} | C_1 = c_1) \prod_{j=1}^{J} P(Y_{2j} = y_{2j} | C_2 = c_2),$$

where $C_1$ represents the latent status at the first wave and $C_2$ represents the latent status at the second wave. The transition probability is represented by $P(C_2 = c_2 | C_1 = c_1, x)$.

In the third part of the model, we related the transition probabilities to covariates of interest (physical and mental health and presence of advance directives) using a logistic regression model for nominal responses. The model incorporates covariates (such as report of having advance directives), denoted by $x$, that are potentially associated with transitions between preferences for specific categories of potentially life-sustaining treatment. The association between a covariate and a transitional probability was expressed as an odds ratio around which we constructed 95% confidence intervals.