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Predictors of Mortality in Nursing Home Residents With Advanced Dementia

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Abstract

This analysis uses data from the Care of Nursing Home Residents with Advanced Dementia (CareAD) study to investigate which factors increase the risk of death in patients who are in the advanced stages of dementia. The hypothesis of this analysis was that specific illnesses with known high mortality would be associated with increased risk of death in the population of nursing home residents with advanced dementia, after controlling for demographic variables and disease-stage variables. Baseline data on 123 end-stage dementia nursing home residents were analyzed with a Cox proportional hazards regression. Of the comorbidities studied, pneumonia was the only illness significantly associated with shortened survival. This information can help health care professionals assist surrogate decision makers in making medical decisions regarding the treatment of comorbid medical illness in persons with advanced dementia.

Keywords

dementia, mortality, comorbid illness, pneumonia, survival analysis

Introduction

The irreversible dementias, which include conditions such as Alzheimer's disease (AD), vascular dementia, and mixed dementia, are progressive, degenerative brain diseases and are most prevalent in the elderly.[1,2] The National Center for Health Statistics ranked AD, the most common cause of dementia, as the eighth leading cause of death in the United States in 2003, and as the seventh leading cause for the years 2004-2006.[3,4] A 1999 study using prevalence data estimated that AD accounted for 7% of all deaths, placing it on par with cerebrovascular disease as the third leading cause of death in the United States.[5] A national study on the place of death for older persons with dementia found that 67% of dementia-related deaths occurred in nursing homes.[6]

Various factors may play a role in determining survival time for individuals with dementia. [7,8] Survival time in dementia has been reported to range from 1 to 13 years.[9] Among the few longitudinal studies that followed community cases of dementia, the estimates of mean survival ranged from 3 to 5.7 years.[9-11] Factors commonly associated with a higher risk of death in dementia are increasing age, male gender, and greater disease severity.[12-15] There are conflicting or inconclusive reports regarding the role of psychiatric symptoms, dementia diagnosis, and comorbid illnesses.[7,11,16-18] Thus, among the more than 30 studies that have investigated predictors of survival in dementia, little consensus has emerged regarding factors that reliably predict the length of time to death for individuals with dementia.[7,12,13]

Variability in survival time has also been reported in studies that examine individuals in the severe disease stage. In 1 study of 11 hospice patients with dementia, all of whom were classified as having severe dementia, the range of survival spanned from 2 days to beyond 16 months.[19] Similarly, in a longitudinal study of 165 nursing home residents who met Medicare hospice criteria, Schonwetter et al,[20] found that the range in survival time was 0 days to 2.13 years. These data support the assertion that individuals with advanced dementia who receive care at a nursing facility can survive for long periods of time and at the same time are at risk of sudden, life-threatening events such as respiratory and urinary tract infections and pressure ulcers, which are difficult to predict.[20,21]

Few studies have examined the contribution of specific medical comorbidities or psychosis as predictors of time to death in a sample of patients who were all judged as being in late-stage dementia. The current analysis uses data from the Care of Nursing Home Residents with Advanced Dementia (CareAD) study to identify factors that increase the risk of death in patients who are in the advanced stages of dementia. We chose to investigate the following medical and

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psychological comorbidities: cardiovascular disease, chronic obstructive pulmonary disease (COPD), diabetes mellitus, pneumonia, and psychosis. The first 3 medical conditions were chosen because they are chronic conditions and are known to decrease life expectency.[22-24] Pneumonia was included because it is estimated to be the most common immediate cause of death in patients with dementia.[25] Psychosis was chosen because of a recent finding that patients who exhibit symptoms of tactile hallucinations die sooner than those who do not.[26] The hypothesis examined in the current analysis is that 1 or more of these illnesses would be associated with increased risk of death in the population of nursing home residents with advanced dementia, after controlling for demographic variables and disease severity variables.

Methods

The CareAD study was a longitudinal, cohort study conducted in 3 Maryland nursing homes from December 2000 to August 2004.[27] The key aims of the study were to document the medical and psychiatric problems and treatment decisions that are faced in end-stage dementia and to identify criteria that predict death within 6 months. The study was approved by the Institutional Review Boards of the Johns Hopkins Medical Institutions and the University of Maryland and by the research review committees at each study site.

The methods of the CareAD study are described in detail elsewhere.[27] In brief, residents from 3 nursing homes were recruited and followed over a period of 3.67 years. Residents were eligible to be enrolled in the study if they (1) had a diagnosis of dementia and (2) met hospice criteria for dementia or were receiving hospice or palliative care. Once a resident was identified as eligible for the study, the resident's surrogate decision maker was contacted and asked for permission to enroll the resident and the surrogate into the study. The enrollment process was congruent with the Alzheimer's Association guidelines for identifying a surrogate decision maker based on Maryland's Health Care Decisions Act, obtaining proxy written consent, and obtaining assent from the participants who were able to provide it.[28] Of the 289 residents identified as eligible for the study, a total of 126 residents were enrolled into the study. In this group of 126, 2 residents did not fully satisfy the eligibility criteria, and a third was withdrawn by the surrogate after 1 month. This analysis uses data on the remaining 123 residents who were followed from baseline to time of death, discharge, or the close of the study.

Residents' demographic data were collected from their medical records and in interviews with their surrogates. Data on residents' medical and psychiatric status were collected by trained research assistants who performed a systematic review of their medical records using a standardized data collection instrument. Baseline data were collected on the presence of any medical and psychiatric problems that occurred during the 6 months prior to the resident's study enrollment or since admission if they had been residing in the nursing home for less than 6 months.

Residents' cognitive status at baseline was tested with the Severe Impairment Rating Scale (SIRS), a 22-point scale for measuring cognitive function in individuals who score 5 or less on the Mini-Mental State Examination.[29,30] It has been shown to have good inter-rater and retest reliability and to correlate with the Mini-Mental State Examination (Pearson $r = .84$) and the Glasgow Coma Scale (Pearson $r = .85$), which have been shown to have satisfactory validity for measuring cognitive impairment in patients with dementia and patients with acute cerebral disorders.[29-33]

Data Analysis

A Cox proportional hazards regression was conducted with Stata software to examine the relationship between survival time with 5 comorbidities: cardiovascular disease, COPD, diabetes mellitus, psychosis, and pneumonia.[34,35] Because some studies suggest that age, gender, and measures of dementia severity influence survival, we included these covariates in the regression analysis. In addition, because the data were collected from 3 different nursing homes, an indicator variable for nursing home site was generated to account for unmeasured differences among the nursing homes.

The data analysis included the following steps: (1) exploratory analysis to describe the data, (2) bivariate analysis using independent t tests and chi-square tests to investigate trends and associations between variables, (3) inspection of Kaplan-Meier graphs and survival time summaries to investigate potential interactions between variables, (4) univariate and multivariate regression analyses with the Cox proportional hazards model, and (5) stepwise regression and likelihood ratio tests to determine the most appropriate model. Both forward and backward stepwise regression techniques were used to determine variables associated with the likelihood of death in the regression model. All variables except nursing home site were tested in the final model. Variables were kept in the final model if they were determined by either the forward or backward stepwise regression procedure to enhance the model's predictive ability. Likelihood ratio tests with a cutoff of $P = .15$ were used to test each next model against the last.

Bootstrapping was used to construct the confidence intervals and P values in the final model. Once the final regression model was derived, regression diagnostics were used to test that the model passed the Cox model assumption of proportional hazards and to verify that possible outlying data points did not have significant influence on the results. A P value less than .05 was considered statistically significant.

Results

Of the 289 residents who were eligible for the study, 123 residents were enrolled. The reasons that residents were not enrolled in the study are as follows: (1) residents died before enrollment could occur (23.2%), (2) surrogates denied permission to enroll residents (17.6%), (3) residents were discharged before enrollment could occur (6.2%), (4) physicians denied

Table 1. Characteristics of Study Participants and Relationship to Survival (n = 123)

Residents' Characteristics	Total Sample	Died (n = 93)	Survived or Discharged (n = 30)	Statistic	*P* value
Demographic characteristics					
Gender					
Female, % (n = 68)	55.3	53.8	60.0	χ^2 (*df* = 1) = 0.357	.550
Male, % (n = 55)	44.7	46.2	40.0		
Age (years), mean(SD) (n = 123)	81.5 (7.1)	82.1 (7.0)	79.6 (7.0)	*t* = −1.705	.095
Race (n = 123)					
White, % (n = 103)	83.7	83.9	83.3	χ^2 (*df* = 1) = 0.005	.945
Non-white, % (n = 20)	16.3	16.1	16.7		
Residence (n = 123)					
Site 1, % (n = 41)	33.3	35.5	26.7	χ^2 (*df* = 2) = 1.068	.586
Site 2, % (n = 60)	48.8	46.2	56.7		
Site 3, % (n = 22)	17.9	18.3	16.7		
Health status characteristics					
Dementia diagnosis (n = 123)					
Alzheimer disease, % (n = 71)	57.7	62.4	43.3	χ^2 (*df* = 1) = 3.367	.067
Other types of dementia,[a] % (n = 52)	42.3	37.6	56.7		
Years with dementia symptoms,[b] mean (SD) (n = 122)	8.6 (5.8)	8.8 (6.0)	7.9 (5.2)	*t* =−0.807	.423
Years at nursing home, mean (SD) (n = 123)	1.9 (3.0)	2.1 (3.3)	1.6 (1.8)	*t* = −1.025	.308
SIRS score, mean (SD) (n = 121)	10.3 (6.7)	10.1 (6.4)	11.1 (7.6)	*t* = 0.660	.513
Health problems[c]					
Heart disease, % (n = 123)	48.0	48.4	46.7	χ^2 (*df* = 1) = 0.027	.870
Pulmonary disorders, % (n = 123)	17.9	18.3	16.7	χ^2 (*df* = 1) = 0.040	.841
Diabetes mellitus, % (n = 123)	13.8	14.0	13.3	χ^2 (*df* = 1) = 0.008	.929
Hallucinations and/or delusions, % (n = 123)	26.8	26.9	26.7	χ^2 (*df* = 1) = 0.0005	.982
Pneumonia, % (n = 123)	25.2	29.0	13.3	χ^2 (*df* = 1) = 2.966	.085

[a] Vascular dementia, mixed dementia, Lewy body dementia, frontotemporal dementia, dementia type not specified, dementia due to HIV, dementia due to Parkinson disease.
[b] Missing data—Years with dementia symptoms (n = 1), Severe Impairment Rating Scale (SIRS) score (n = 2).
[c] Health problems reported in medical records during 6 months preceding enrollment.

permission to recruit residents (4.8%), and (5) surrogates could not be contacted despite multiple attempts (4.5%). Enrolled residents were more likely than the nonenrolled to be female ($\chi^2 = 4.401$, $df = 1$, $P = .036$), white ($\chi^2 = 9.105$, $df = 1$, $P = .003$), and to have a female surrogate ($\chi^2 = 5.321$, df=1, $P = .021$).

Descriptive data on the nursing home residents are displayed in Table 1. At baseline, the mean age of the residents was 81.5 (SD 7.1), 55.3% were females, and 83.7% were white. The majority of residents had a diagnosis of AD (57.7%). The median years with symptoms of dementia was 8 (range: 0-33); the median SIRS score was 11 (range: 0-22).

Of the 123 residents in this sample, 93 died, 7 were discharged from the facilities and alive at the final interview, and 23 were living in the nursing homes at the final interview. As shown in Table 1, there were no significant differences in terms of gender, age, race, site, years with symptoms, years at nursing home, SIRS score, or comorbidity between those who died and those who did not. There was a trend for participants with non-AD types of dementia to be alive (χ^2 =3.367, $P = .067$).

Residents were followed on average for 60.8 weeks. (The total follow-up time for the sample was 7477 person weeks.) The median survival time overall was 43.6 weeks, and the overall incidence rate was 0.012 deaths per person week. The Kaplan-Meier survivor function estimated that for a nursing home resident in this study, the probability of surviving beyond 6 months is 68.0%, and the probability of surviving beyond 1 year is 48.6%.

Table 2 displays the results from the univariate and multivariate Cox proportional hazards regression analyses. In the univariate analysis, pneumonia ($P = .008$) was significantly associated with decreased survival but heart disease, pulmonary disorder, diabetes mellitus, and psychosis were not. The univariate model estimated that subjects who had a history of pneumonia in the 6 months leading up to enrollment were at 2.10 times greater risk of death compared to those with no 6-month history of pneumonia (95% CI: 1.21-3.65). Nursing home site was also found to have a statistically significant relationship with the risk of death. Additionally, the results from the univariate analysis suggest that the type of dementia could have an association with the risk of death ($P = .09$).

To further examine statistically significant findings from the univariate analysis, a multivariate regression analysis was performed to control for all variables. Similar to the results in univariate model, this full model estimated that pneumonia would increase a participant's risk of death by 2.06 times (95% CI:

Table 2. Crude and Adjusted Relative Hazard of Mortality (n = 123)

	Univariate Analyisis[a](n = 123)			All Covariates (n = 120)			Final Model[b] (n = 120)		
	HR	95% CI	*P* Value	HR	95% CI	*P* Value	HR	95% CI	*P* Value
Site 2[c]	0.62	0.41-.96	.03	0.63	0.27-1.45	.28			
Site 3[c]	0.49	0.26-.92	.03	0.39	0.12-1.29	.12			
Female gender	0.72	0.47-1.09	.12	0.96	0.43-2.15	.92	0.69	0.41-1.15	.15
Age [d]	1.02	0.98-1.05	.32	1.04	0.99-1.10	.14	1.03	0.98-1.08	.25
Years at nursing home[e]	0.97	0.90-1.04	.37	1.02	0.90-1.15	.80			
Mixed or other dementia	0.69	0.45-1.06	.09	0.57	0.30-1.09	.09	0.59	0.35-1.00	.05
Psychosis	1.12	0.71-1.76	.62	1.03	0.50-2.11	.94			
Pulmonary disorders	1.43	0.80-2.57	.23	0.96	0.42-2.18	.92			
Diabetes mellitus	1.32	0.65-2.67	.44	1.74	0.79-3.80	.17			
Pneumonia	2.10	1.21-3.65	<.01	2.06	0.93-4.56	.08	2.23	1.19-4.20	.01
Heart Disease	1.23	0.81-1.87	.34	1.27	0.69-2.33	.45			
SIRS score 6-13[f] (n = 121)	1.26	0.74-2.15	.39	1.40	0.63-3.13	.41	1.43	0.76-2.69	.27
SIRS score 14+[f] (n = 121)	0.83	0.47-1.46	.52	0.72	0.29-1.81	.48	0.80	0.38-1.66	.55
7 + years with symptoms[g] (n = 122)	0.80	0.52-1.23	.30	0.68	0.36-1.30	.24	0.76	0.46-1.27	.30

[a] Missing data—SIRS scores (n = 2), years since dementia symptoms began (n = 1).
[b] Final model includes gender, age, site, Severe Impairment Rating Scale (SIRS), dementia type, pneumonia, diabetes mellitus, and years with dementia symptoms.
[c] Reference category: Site 1
[d] With every 1 year increase from mean age (81.5 years)
[e] With every 1 year increase from mean years in nursing home (1.9 years)
[f] Reference category: SIRS score 0-5
[g] Reference category: 0-6 years with symptoms

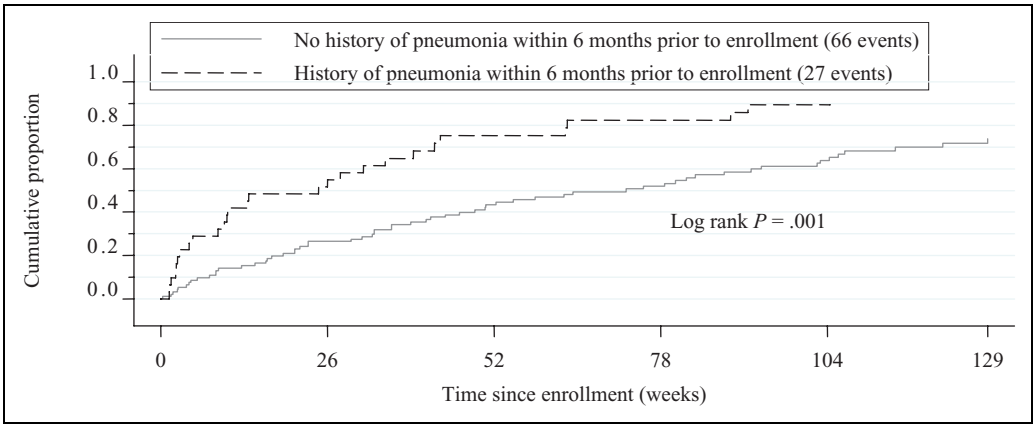

Figure 1. Kaplan-Meier estimation of cumulative proportion of nursing home residents who died.

0.93-4.56), although this effect was no longer statistically significant at the .05 level (P =.08). The estimates of the risk of death by dementia type and nursing home site were also consistent with the results of the univariate analysis.

The final model reveals a statistically significant difference in the risk of death comparing residents by history of pneumonia and by dementia type. Specifically, the model estimates that the risk of death at a given day for a resident who was diagnosed with pneumonia within the 6 months leading up to enrollment is 2.23 times the risk for a resident with no 6-month history of pneumonia (95% CI: 1.19-4.20, P = .01). The risk of death for a resident with mixed or other non-AD dementias is estimated to be reduced by 41% compared to the risk of residents with a diagnosis of AD (95% CI: .35-1.00, P = .05).

Figure 1 presents the Kaplan-Meier estimation of survival in participants who had or had not been diagnosed with pneumonia during the 6 months prior to enrollment. Residents with pneumonia had a 54.8% chance of dying within 6 months, whereas those without pneumonia had a 26.4% chance (log rank χ^2 = 10.86, P = .001). Table 3 summarizes the median survival times for residents by diagnosis. The median survival for participants with Alzheimer's dementia was 42.14 weeks compared to 83.43 weeks for participants with mixed dementia and other dementia.

Table 3. Comparison of Median Survival by Diagnosis

Diagnosis	Median Survival (weeks)
All participants	50.57
No history of pneumonia[a]	72.57
History of pneumonia[a]	24.57
Alzheimer's dementia	42.14
Mixed dementia and other dementias	83.43

[a] Within 6 months prior to enrollment.

Discussion

This study of individuals with dementia who were hospice eligible found that pneumonia occuring during the 6 months prior to enrollment, but not heart disease, pulmonary disorders, diabetes, hallucinations or delusions, was significantly associated with decreased survival time controlling for gender, age, dementia type, SIRS score and years with dementia symptoms, and that participants diagnosed with AD were more likely to die than individuals with a diagnosis of mixed or other dementia. In this sample, individuals who had been diagnosed with pneumonia within the 6 months prior to their enrollment were at 2.23 times greater hazard of death than those without a pneumonia diagnosis. Individuals who had mixed or other dementias had an estimated 41% lower adjusted risk of death than those with Alzheimer's dementia.

Given the fact that pneumonia has been found in several death certificate and autopsy studies to be the leading cause of death in patients with dementia, it is not surprising that we found that residents with a baseline diagnosis of pneumonia had significantly decreased survival time compared to those who did not.[25,36,37] However, we did not examine documentation for cause of death, so we cannot conclude that the participants died of pneumonia.

A more complex question prompted by this finding is whether pneumonia can be reliably used in making a prognosis of time to death in this patient population. Thus far, of the studies that have concentrated on prognostic factors for death in patients with advanced dementia, pneumonia is not consistently found to be a reliable predictor. In the retrospective study of 2 large groups of nursing home residents (n = 11 430), Mitchell et al[38] did not find substantial evidence that a diagnosis of pneumonia should be used to predict death within 6 months. It should be noted, however, that only a small portion of that sample was diagnosed with pneumonia, so it is possible that a predictive effect would not have been captured in statistical analysis. In a prospective study of 165 hospice patients with dementia, Schonwetter et al[20] found that patients with pneumonia were not significantly more likely to die within 6 months of study enrollment. Contrastingly, pneumonia was identified by van der Steen et al[17] to be a signficant predictor of death in a prospective study of 944 nursing home residents with various stages of dementia. In their study, over one third of the residents who developed a diagnosis of pneumonia died within 6 months of their diagnosis.

Recently, Mitchell et al identified pneumonia, in addition to febrile episodes and eating problems, as a complication that occurs frequently and acts as a harbinger of death in individuals with advanced dementia, and we reexamined our data in light of these findings.[39] Similar to Mitchell's sample, we found a high prevalence of eating problems at baseline (84.6%). However, in univariate analysis, we did not find that the presence of an eating problem significantly predicted death (HR: 0.983, 95% CI: 0.55-1.75). We did not collect data on the occurence of febrile illnesses in our sample. We did code whether our participants were reported to have a fever, but the low rate at baseline (4.9%) precluded its inclusion as a variable in a survival analysis.

Because residents with pneumonia in this study were only modestly more at risk of death (2.25 times) compared to other comparable residents, we suggest that those making medical decisions for persons with advanced dementia be told that the risk of death is modestly increased after pneumonia has occurred. Looked at another way, the median survival time for those with a history of pneumonia was 25 weeks compared to 73 weeks for those without pneumonia. Stating the data this way may help convey the information that a diagnosis of pneumonia is associated with a meaningfully shortened life expectancy in this population of nursing home residents with advanced dementia.

In this analysis, residents with vascular dementia, mixed dementia, or other types of dementia had a lower risk of death compared to those residents with AD. Of the previous few studies that have investigated differences in survival between AD and other types of dementia, the results have been mixed.[7,9,40,41] In a study of community residents with incident dementia cases, Fitzpatrick et al[40] found that persons with vascular dementia were at greater risk of death than those with AD and mixed dementia. Their study also found that participants with mixed and vascular dementia had higher prevalence of coronary artery disease, hypertension, and history of stroke.[40] Mortel et al[41] found that survival times were similar among both patients with vascular dementia and AD, when patients underwent treatment of risk factors for cerebrovascular disease. It is possible that participants in this study were receiving vigilant care for cerebrovascular disease risk factors such as hypertension, heart disease, and hyperlipidemia, which could prolong survival time. It is also plausible that those patients with the highest degrees of these risk factors may have died earlier in the illness and that the results demonstrate a survivor bias.[42]

Gambassi et al previously investigated the role of comorbidity in the mortality of nursing home residents with dementia and found that COPD, heart disease, and diabetes each modestly increased residents' risk of death.[14] Although we calculated effect sizes similar to those in the Gambassi et al study,[14] the results were not statistically significant. The reason for this may be that we did not have an adequate sample size to detect whether these modest effect sizes had a statistically significant effect on the risk of death. Other possible explanations for our results include (1) survivor bias, (2) better medical

treatment in the controlled environment of long-term care facilities, or (3) an overwhelming effect of pneumonia alone.

Another factor regarding medical comorbidity, which we were not able to investigate but which warrants further study is the possibility that health problems interacted with one another in participants who had more than 1 health problem. This study did not have a large enough sample size to test the combined effect of diabetes and heart disease or heart disease and vascular dementia.

In this analysis, age was not found to be a significant predictor of death. To the best of our knowledge, there have been only 2 other studies that have examined the effect of age on the risk of death in samples of patients with specifically advanced dementia. In a sample of 165 hospice patients, age was not found to be a significant predictor of death when analyzed in a univariate Cox regression analysis. Age did have a small effect on risk of death (RR: 1.03, CI: 1.01-1.06), when it was included in a model that accounted for anorexia and function, suggesting that there was an association between age and one or both of those added measures. [20] In a very large sample of 6799 nursing home residents, residents who were older than 83 years were found to be at 40% increased risk of death compared to younger residents (95% CI: 1.3-1.6). However, functional status and medical comorbidities had stronger effects on the risk of death.[38] The finding that age does not influence mortality in our study likely reflects the fact that disease variables are predominant over the usual relationship between older age and increased risk of death.

Even though all participants in this study either met current criteria for receiving hospice care or were judged by their physician to be likely to die within 6 months, survival times covered a much broader range (interquartile range [IQR]: 17-122 ?thyc=5?> weeks) than we had anticipated. The Kaplan-Meier survivor function estimated that the probability of surviving beyond 6 months is 66.4% and the probability of surviving beyond 1 year is 48.6%. The residents in this sample tended to survive longer than residents in 2 studies of similar samples, where the majority of patients died within 6 months.[19,20] This may be explained by the fact that our sample was taken from a nursing home population whereas the patients in the other two studies were residing in hospice facilities. In both this study and in Schonwetter's[20] sample, there is a consistent finding that a subset of patients with end-stage dementia will survive far longer than predicted, beyond 2 years.

Multiple limitations to this study should be noted. First, of the 289 residents who were eligible for the study, only 123 were enrolled. Our findings may have differed if the 23.2% of the nonenrolled group who died before enrollment had been included. Furthermore, participants who were enrolled were more likely to be female. Because there are studies that suggest that males are at greater risk of death in dementia,[12] male-associated mortality may have been underestimated. A second limitation of our sample is that 2 demographic factors, gender and site, were not independent of one another. Because gender was unevenly distributed across nursing home sites, this limited our ability to determine if gender was an independent risk factor. A third limitation of the sample is that there may have been interactions between predictors that our sample size was too small to detect. A limitation regarding our data collection is that the participants' advanced state of impairment did not allow for the collection of standardized functional status data. Finally, because this study included individuals residing in only 3 facilities in a single limited geographic area, generalization to residents in other geographic areas should be made with caution.

Dementia is a leading cause of death in the United States, and the majority of dementia-related deaths occur in nursing homes.[3,4,6] Two recent qualitative studies found that a recurring theme in surrogate decision makers' experiences are deficiencies in surrogates' understanding of the disease trajectory of dementia and lack of communication with the treating health care professionals.[43,44] Knowledge of events in late-stage dementia that influence time to death might aid families in their surrogate decision-making experience.[44] We recommend that health care professionals assist surrogate decision makers by conveying how pneumonia may affect the prognosis of a patient with dementia.

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Declaration of Conflicting Interests

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