Predictors of mortality in patients with Alzheimer's disease living in nursing homes

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Abstract

***Objectives*—To identify factors associated with mortality in patients with Alzheimer's disease, and to evaluate whether these factors vary according to severity of cognitive impairment.**

***Methods*—Data were from the SAGE database which includes information on all residents admitted between 1992 and 1995 to all Medicare/ Medicaid certified nursing homes of five US states. We conducted a longitudinal follow up study (median 23 months) on 9264 patients aged 65 years and above with a diagnosis of Alzheimer's disease. Patient data including demographic characteristics, dementia severity, comorbidity, and other clinical and treatment variables were collected with the Minimum Data Set. Information on death was derived through linkage to Medicare files. Baseline characteristics were used to predict survival in univariate and multivariate Cox proportional hazard models.**

***Results*—Overall mortality rate was 50%, with a first year rate of 25.7%. Increased age (risk ratio (RR) 1.83; 95% confidence interval (95% CI) 1.65–2.03, for patients 85+ years), male sex (RR 1.81; 95% CI 1.70–1.94), limitation in physical function (RR 1.45; 95% CI 1.27–1.66), a condition of malnutrition (RR 1.31; 95%CI 1.23–1.39), the presence of pressure ulcers (RR 1.24; 95% CI 1.13–1.36), a diagnosis of diabetes mellitus (RR 1.32; 95% CI 1.21–1.43), and of cardiovascular diseases (RR 1.22; 95% CI 1.14–1.30) were independent predictors of death, regardless of the severity of baseline dementia. Sensory problems (hearing and vision) and urinary incontinence were associated with increased mortality only among patients with less severe dementia. The presence of disruptive behaviour, aphasia, and a diagnosis of Parkinson's disease were not related to survival. African-Americans and other minority groups were less likely to die relative to white people.**

***Conclusions*—Age, sex, functional limitation, and malnutrition seem to be the strongest predictors of death for patients with Alzheimer's disease in nursing homes. Altogether, severity of dementia has no influence on survival, yet the predictive role of certain variables depends on the degree of impairment. Minority groups have a reduced risk of death relative to white people.**

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Alzheimer's disease is the most common form of dementia, and a major healthcare problem.[1 2] Recent evidence suggests that the prevalence of Alzheimer's disease is about 50% in people older than 85 years.[3] In the United States, it is estimated that Alzheimer's disease afflicts nearly 4 million people and is the fourth leading cause of death.[4]

Although estimates of the risk of death among those with Alzheimer's disease have varied greatly, most studies, both institutional[5–7] and community based,[8–14] have suggested that it is substantially increased relative to age and sex matched control subjects.

Several factors seem to contribute to mortality of patients with Alzheimer's disease. These include increasing age,[7 8 15–19] male sex,[7 13 17–20] and functional disability.[6 14 17 21 22] Some studies, but not all, have found the risk of mortality to be associated with extrapyramidal signs,[20 23–25] psychiatric symptoms,[23 26 27] depression,[28] nutritional indices,[7 10 11 29 30] language loss and aphasia,[31 32] and apolipoprotein phenotype.[33] The effect of severity of dementia on survival of patients with Alzheimer's disease is inconsistent; an almost equal number of studies have shown an association,[7 9 11 13 14 16 17 34] or no relation.[18 19 22 27 32 35] Few of these studies have controlled for the potential impact of comorbid conditions[7 9 13 14 19 21] and the results remain inconclusive. Likewise, race was rarely considered in studies of survival of patients with Alzheimer's disease.[8 17 36]

Thus, despite more than 100 reports describing the predictors of survival among patients with Alzheimer's disease, we remain unable to identify risk profile and to estimate reliably the length of time to death. Providing an empirically based answer would have far reaching consequences, as Alzheimer's disease has a profound effect also on the million formal and informal caregivers who assist these patients. Even more relevant would be the impact on long term care facilities where most of these patients live.

The purpose of the present study was to examine predictors of survival in a large sample of patients with Alzheimer's disease living in United States nursing homes. Specifically, we determined the role of comorbid conditions affecting these patients on survival, and evaluated whether this varies by severity of dementia.

Methods

SAGE DATABASE

We used data from the SAGE (Systematic Assessment of Geriatric drug use via Epidemiology) database, which has been described in detail elsewhere.[37–39] The SAGE is a population based, longitudinal database (1992–5) that comprises data collected with the Minimum Data Set (MDS) on residents of the nursing homes in five states (Kansas, Maine, Mississippi, New York, and South Dakota) and data on the medications used by each resident. These data have been cross linked to Medicare eligibility files to retrieve information on vital status.

The MDS is an assessment instrument that contains more than 300 items describing demographic, functional, and clinical characteristics of each resident.[40] An extensive array of symptoms, syndromes, and treatments is also included, and indicators describing resident's behaviour, mood, and involvement in activities. Among others, two summary scales based on MDS items describe the level of cognitive function (cognitive performance scale (CPS))[41] and residents' performance in activities of daily living (ADL scale).[42] The validity and reliability of these summary scales have been previously documented.[43] The diagnoses of all comorbid conditions were coded by the staff physician or assistant physician consulting transfer documentation and medical records. The overall validity and accuracy of the diagnostic information contained in the SAGE database has been documented by reviewing Medicare's hospital discharge claims.[39] Furthermore, elements of the SAGE database have been used in other epidemiological studies.[44–46]

STUDY POPULATION

We selected residents newly admitted to nursing homes with a diagnosis of probable Alzheimer's disease. The key criteria of the diagnostic and statistical manual of mental disorders (DSM-IV) were used for the definition of Alzheimer's disease.[47] In interrater and test-retest trials, diagnosis of Alzheimer's disease showed an excellent κ coefficient (0.81), and proved of research value.[48 49] Patients were at least 65 years of age at their initial MDS assessment, and we excluded patients with a history of mental retardation, mental illness or any other life long mental health disorders. This strategy yielded a sample of 9264 patients.

ANALYTICAL APPROACH

All demographic variables, measures of severity of dementia and comorbid conditions were gathered at initial MDS assessment on admission to the nursing home. Demographic variables included age, sex, race, and marital status. Measure of physical function was based on activities of daily living scores and severity of dementia was based on CPS scores. Psychological status was measured investigating whether residents showed any observable signs or indicators of delirium (less alert, changing awareness of environment, incoherent speech, lethargy, changing of cognitive ability over the course of a day).[40] Residents were considered to have behaviour problems when they exhibited wandering or socially inappropriate or disruptive behaviour, or they were verbally or physically abusive.[40] Comorbid conditions included cardiovascular diseases, stroke, aphasia, diabetes mellitus, malnutrition, chronic obstructive pulmonary disease, depression, Parkinson's disease, and sensory impairment affecting the ability to hear or read. Cardiovascular comorbid conditions (ischaemic heart disease, congestive heart failure, hypertension, arrhythmia) were evaluated both separately and as a combined variable. We considered body mass index, calculated using residents' body weight and height collected in the MDS, as a marker of nutritional status. This measure has shown good validity when compared with anthropometric variables.[50] We also evaluated the presence of urinary incontinence, of pressure sores, and of history of falls or of use of restraints. Most variables were categorised as present or not present when examining their main effect on survival. Age was stratified in 10 year intervals, 65–74, 75–84, and 85+. ADL scores were used to group patients in three clinically meaningful strata; a score of 0–1 was for normal functioning, a score of 2–3 identified those needing supervision, and a score of 4–5 were those who required extensive assistance in performing basic activities of living. A CPS score of 2 to 4 was considered moderate cognitive impairment, and a score of 5–6 was judged as severe impairment. These values compare with widely accepted cut offs on the mini mental state examination scale.[43]

We performed a survival analysis using Cox proportional hazards modelling. Time to death was calculated from the date of first MDS assessment to the date of death. Information on

Table 1 General characteristic of study population (n=9264)

Characteristic	*%*
Age (y):	
65-74	14.4
75-84	48.6
85+	37.0
Sex:	
Female	69.2
Race:	
White	90.7
African—Americans	6.5
Others*	2.8
Marital status:	
Married	34.3
Widowed	54.6
Other†	11.0
Physical function (ADL score)‡	
Normal	12.0
Need supervision	45.1
Require assistance	42.9
Cognitive function (CPS score)§	
Normal/minimal	6.6
Moderate impairment	58.7
Severe impairment	34.7
Advanced directives:	
Do not resuscitate	40.0
Malnutrition (BMI <21 Kg/m^2)¶	41.9
Number of diagnoses:	
None	11.9
1-2	45.3
3-4	30.6
5+	12.3

*Includes Asian/Pacific islander, Hispanic, American Indian/Alaska native; †includes never married and divorced/separated; ‡activities of daily living; §cognitive performance scale;¶body mass index.

Table 2 Crude and adjusted relative risks (RRs) of mortality

	Dead/alive (No of patients)	*Crude model (RR (95% CI))*	*Adjusted model (RR (95% CI))*
Age *(y)*:			
65-74	513 / 822	—	—
75-84	2121 / 2377	1.34 (1.22 - 1.47)	1.34 (1.22 - 1.48)
85+	1997 / 1434	1.84 (1.67 - 2.03)	1.83 (1.65 - 2.03)
Sex:			
Female	2790 / 3612	—	—
Male	1831 / 1020	1.82 (1.72 - 1.93)	1.81 (1.70 - 1.94)
Race / ethnicity:			
White	4222 / 4031	—	—
African-American	248 / 340	0.81 (0.71 - 0.92)	0.82 (0.72 - 0.94)
Other minorities	99 / 160	0.68 (0.56 - 0.83)	0.69 (0.57 - 0.85)
Marital status:			
Widowed	2403 / 2645	—	—
Married	1765 / 1412	1.28 (1.21 - 1.36)	1.04 (0.97 - 1.12)
Other	455 / 569	0.97 (0.83 - 1.12)	0.86 (0.75 - 0.97)
Cognitive function:			
Normal	284 / 328	—	—
Moderate impairment	2562 / 2858	1.04 (0.92 - 1.17)	1.04 (0.91 - 1.17)
Severe impairment	1771 / 1430	1.32 (1.17 - 1.49)	1.13 (0.99 - 1.29)
Behaviour problems:			
No	2482 / 2335	—	—
Yes	2124 / 2294	0.91 (0.86 - 0.96)	0.93 (0.88 - 1.00)
Indicators of delirium:			
No	3606 / 3812	—	—
Yes	960 / 750	1.20 (1.11 - 1.28)	1.17 (1.09 - 1.27)
Use of restraints:			
No	3595 / 3954	—	—
Yes	103/ 674	1.39 (1.29 - 1.49)	1.03 (0.95 - 1.11)
Physical function:			
Normal	386 / 719	—	—
Need supervision	1943 / 2211	1.56 (1.40 - 1.74)	1.25 (1.11 - 1.41)
Require assistance	2272 / 1678	2.18 (1.96 - 2.43)	1.45 (1.27 - 1.66)
Hearing problems:			
No	4019 / 4252	—	—
Yes	581 / 377	1.44 (1.32 - 1.58)	1.10 (1.00 - 1.21)
Vision problems:			
No	3816 / 4099	—	—
Yes	700 / 467	1.42 (1.32 - 1.58)	1.13 (1.03 - 1.23)
Urinary incontinence:			
No	1510 / 2137	—	—
Yes	3099 / 2482	1.59 (1.50 - 1.69)	1.15 (1.06 - 1.24)
Pressure ulcers:			
No	4020 / 4284	—	—
Yes	606 / 345	1.64 (1.50 - 1.78)	1.24 (1.13 - 1.36)
Cardiovascular disease:			
No	3056 / 3437	—	—
Yes	1575 / 1196	1.36 (1.28 - 1.44)	1.22 (1.14 - 1.30)
Stroke:			
No	4140 / 4244	—	—
Yes	491 / 389	1.20 (1.10 - 1.32)	1.05 (0.96 - 1.16)
Aphasia:			
No	4547 / 4583	—	—
Yes	84 / 50	1.35 (1.09 - 1.68)	1.12 (0.89 - 1.40)
Parkinson's disease:			
No	4351 / 4403	—	—
Yes	280 / 230	1.16 (1.03 - 1.31)	0.98 (0.86 - 1.10)
Depression:			
No	2838 / 2909	—	—
Yes	1793 / 1724	1.04 (0.98 - 1.10)	1.11 (1.04 - 1.18)
COPD:			
No	4168 / 4335	—	—
Yes	463 / 298	1.41 (1.28 - 1.55)	1.26 (1.14 - 1.39)
Diabetes mellitus:			
No	3962 / 4130	—	—
Yes	669 / 503	1.27 (1.17 - 1.38)	1.32 (1.21 - 1.43)
Malnutrition (BMI < 21):			
No	2420 / 2875	—	—
Yes	2126 / 1689	1.35 (1.27 - 1.43)	1.31 (1.23 - 1.39)
Falls:			
No	2883 / 3067	—	—
Yes	1714 / 1537	1.16 (1.09 - 1.23)	1.01 (0.96 - 1.07)

COPD=chronic obstructive pulmonary disease.

date of death was derived by linking patients with the Medicare enrollment files via the health claim number present in the MDS form. We examined all events which occurred through March 1997, with a median follow up of 23 months (range 1–58). Each baseline characteristic was considered in separate proportional hazards models. Prognostic factors identified in the univariate analyses were then candidates for inclusion in the final models where we adjusted for potential confounders. We considered confounders as any variable that altered the measure of effect of interest by more than 10%. Age and sex were considered important confounders of the association between prognostic factors and survival and were always included in the adjusted models. We assessed and ruled out multicollinearity. This modelling approach was also performed stratifying patients in two groups based on CPS scores, 2 to 4 (moderate impairment), and 5–6 (severe impairment). Hazard rate ratios (RRs) and corresponding 95% confidence intervals (95% CIs) were derived from the final models. All analyses were performed using SAS version 6.12 (Cary, NC, USA).

Results

Table 1 lists the principal baseline demographic characteristics of the sample. Patients were 82.1 (SD 6.8) years old, with over 85% aged 75 years and above. Nearly 70% of patients were women and white patients comprised the overwhelming majority (91%) of the population. Patients had 2.5 (SD 1.8) clinical diagnoses other than Alzheimer's disease, and showed a high degree of functional impairment as indexed by the difficulty in performing activities of daily living. Forty two per cent had a BMI value <21 kg/m^2. Whereas about 6% of the patients had only a minimal impairment of cognitive function, over a third (35%) scored 5 or 6 on the CPS scale—that is, severe dementia.

During a median follow up of 23 months, 4631 patients (50%) died; 26% dying within the first year. Table 2 presents both the crude and adjusted relative risks for each of the variables considered in this study. At univariate analysis, increased age and male sex were associated with a greater risk of mortality. Among the indices describing the overall clinical severity, limitation in physical function, presence of pressure ulcers, of urinary incontinence, use of restraints, and indicators of delirium were all associated with an increased risk. Most of the comorbid conditions considered were associated with increased mortality. These included sensory impairment (hearing and vision problems), respiratory diseases, cardiovascular diseases, aphasia, diabetes mellitus, and malnutrition.

After adjustment, age, sex, functional limitation, malnutrition, diabetes mellitus, COPD, pressure ulcers, and cardiovascular diseases remained associated with increased mortality. Minority patients were less likely to die during the follow up relative to white patients (RR=0.81 for African-Americans and RR=0.68 for patients belonging to other race groups). This association persisted after adjustment for age, sex, level of impairment, and all concomitant conditions.

Table 3 shows the results of a stratified analysis to evaluate whether factors related to mortality differed by baseline cognitive impairment. Advanced age, male sex, limitation in physical functioning, malnutrition, presence of pressure ulcers, and a diagnosis of diabetes mellitus and of cardiovascular diseases were independent risk factors for mortality regard-

Table 3 Adjusted relative risks (95% CI), by baseline level of cognitive impairment

	Moderate (n=5393)	*Severe (n=3160)*
Age (y):		
65-74	—	—
75-84	1.40 (1.21 - 1.62)	1.29 (1.12 - 1.49)
85+	1.77 (1.52 - 2.05)	1.92 (1.65 - 2.23)
Sex:		
Female	—	—
Male	1.94 (1.79 - 2.11)	1.80 (1.63 - 1.99)
Race / ethnicity:		
White	—	—
African-American	0.72 (0.60 - 0.87)	0.99 (0.81 - 1.20)
Other minorities	0.69 (0.52 - 0.92)	0.64 (0.47 - 0.87)
Behaviour problems:		
No	—	—
Yes	0.99 (0.91 - 1.08)	0.85 (0.76 - 0.94)
Indicators of delirium:		
No	—	—
Yes	1.15 (1.03 - 1.27)	1.19 (1.06 - 1.33)
Physical function:		
Normal	—	—
Need supervision	1.26 (1.10 - 1.45)	1.66 (1.10 - 2.53)
Require assistance	1.44 (1.22 - 1.69)	1.98 (1.29 - 3.03)
Hearing problems:		
No	—	—
Yes	1.12 (1.00 - 1.27)	1.06 (0.94 - 1.26)
Vision problems:		
No	—	—
Yes	1.20 (1.05 - 1.36)	1.06 (0.97 - 1.22)
Urinary incontinence:		
No	—	—
Yes	1.16 (1.06 - 1.28)	1.09 (0.95 - 1.28)
Pressure ulcers:		
No	—	—
Yes	1.26 (1.10 - 1.45)	1.23 (1.08 - 1.40)
Cardiovascular disease:		
No	—	—
Yes	1.24 (1.14 - 1.35)	1.21 (1.10 - 1.34)
Depression:		
No	—	—
Yes	1.07 (1.00 - 1.17)	1.19 (1.07 - 1.32)
COPD:		
No	—	—
Yes	1.28 (1.13 - 1.45)	1.18 (1.00 - 1.42)
Diabetes mellitus:		
No	—	—
Yes	1.27 (1.14 - 1.42)	1.36 (1.19 - 1.57)
Malnutrition (BMI < 21):		
No	—	—
Yes	1.33 (1.22 - 1.44)	1.30 (1.17 - 1.43)

COPD=chronic obstructive pulmonary disease.

less of the severity of baseline cognitive impairment. A diagnosis of depression seemed to be a stronger predictor among patients with severe Alzheimer's disease at baseline. By contrast, sensory problems and urinary incontinence were associated with mortality if baseline cognitive impairment was only moderate. Minority groups had a consistently lower risk of mortality regardless of severity of dementia, with the exception of African-Americans with severe impairment.

The presence of any of the four behavioural problems assessed in the MDS (wandering, verbally or physically abusive, socially inappropriate) showed a trend towards inverse relation with mortality (table 2 and 3). When we examined specific domains separately, patients with Alzheimer's disease who showed wandering had a lower rate of mortality than those without such a behaviour problem (44% *v* 53%). By contrast, mortality rate was higher among patients exhibiting severe and aggressive behaviours (53%).

Discussion

The present study shows that among patients with Alzheimer's disease living in long term care facilities increased mortality was related to advanced age, male sex, limitation in physical functioning, malnutrition, presence of pressure ulcers, a diagnosis of diabetes mellitus, and of cardiovascular diseases. These factors were independent predictors of mortality regardless of the severity of cognitive impairment. A diagnosis of depression seemed to be a stronger predictor among patients with severe Alzheimer's disease at baseline. Instead, sensory impairment and urinary incontinence were associated with an increased risk of mortality among patients with only moderate cognitive deficits. Minority groups, both African-Americans and other race or ethnic groups, had a lower risk of mortality, independently of severity of dementia.

In recent years, significant advances have been made in the understanding of Alzheimer's disease, yet effective treatment is not available and the progressive course of the disease cannot be reversed. Thus, considerable attention has been devoted to studies on the early mortality associated with dementia of Alzheimer type in an attempt to identify prognostic factors. Over 100 articles have described several predictors, yet studies have been incomplete and have generated inconclusive results.

We found that increased age, male sex, and white race carried an increased risk of mortality. That increased age was a prognostic factor confirms the great majority of studies published,[16–18] most specifically those including very old patients such as ours, both in the community[19] but especially in nursing homes.[7 15 34 51] The notion that men with Alzheimer's disease have a substantially increased risk of mortality relative to age matched women with disease is the most consistent finding across two decades of research[7 13 17–20]; only two studies were unable to document a sex difference.[8 35] Yet, possible explanations for this difference remain speculative.[52 53] Our study is among the very few that could explore the role of different race or ethnicity. The finding of an increased risk of mortality among white people is in agreement with the paper by Chandra *et al*[36] who searched all death certificates for the years 1971 and 1973 through 1978. However, two other studies in patients with Alzheimer's disease did not find any race difference.[8 17]

Our analysis documented that physical dependency and other measures of debility (presence of pressure sores and urinary incontinence) are among the best predictors of mortality regardless of degree of cognitive impairment. We have used the activities of daily living scale and found similar results as in two previous studies[22 54]; yet a recent article by Aguero-Torres *et al*[19] failed to confirm activities of daily living dependency as a risk factor among patients with Alzheimer's disease. None the less, the last is the only study at variance with the literature. Measures of disability that have been associated with increased mortality in other studies include the Blessed DRS,[14 17 32] the clinical dementia rating scale,[28] decreased grip strength,[8] and severe physical impairment, unstable gait, and falls.[6] This supports the hypothesis that functional decline can have a

course independent of cognitive failure, and that more general rather than specific indicators of the disease status identify high risk patients in nursing homes,[55] just as in hospitals.[56]

We found that selected comorbid conditions (cardiovascular diseases, diabetes mellitus, and COPD) predicted higher mortality, and the association remained regardless of different levels of cognitive impairment. Composite indices of comorbidity have been inconsistently associated with mortality in demented patients.[6 9 19 21] Previous works specifically on vascular diseases found an association with hypertension,[8] cardiovascular diseases,[7 13 14] and myocardial ischaemia,[10] but the findings are not universal.[7 8 14 26] Similarly, non-vascular comorbid conditions were associated with mortality in some studies,[6 7] but not in others.[9 14 21] These different results may be attributable to an underrepresentation of comorbid conditions among demented patients.[48 57] In agreement with the results of other authors,[7 9 14] sensory impairment affecting vision and hearing was associated with a slightly increased risk of mortality in our study. However, these measures are properly markers for general disability and they do not influence mortality directly.

We could not document an association between severity of dementia and mortality. Although this is an area of intense research, an equal number of studies have shown an association,[7 9 11 13–17 34] or no relation,[18 19 22 27 32 35] with mortality of patients with Alzheimer's disease. A clear reason for such disparate findings is elusive but hypotheses have been formulated. On the one hand, the difficulty of ascertaining the age at onset of dementia may attenuate the effect of cognitive decline on survival.[14] This time dependent predictability of severity of dementia would depend on a non-linear course of Alzheimer's disease.[57 58] Alternatively, models simultaneously adjusting for measures of disability that reflect not only functional ability but the general status of the patient might blunt the effect of severity of dementia.[19 22] Finally, clinicopathological studies in patients with Alzheimer's disease have shown that advanced age at death is associated with somewhat less severe dementia and fewer senile plaques and neurofibrillary tangles.[59] Specific areas of cognitive dysfunction, such as verbal fluency or aphasia, have been identified as predictors of mortality.[10 17 32] In our cohort there seemed to be a positive trend, but in agreement with other authors,[14 28] aphasia was not independently associated with increased mortality. Similarly, our findings concur with recent evidence showing no,[7 20 23] or inverse [14] relations between behavioural problems and mortality. The "protection" afforded by wandering is likely due to the fact that it is a marker of better physical function.[60]

Several indices correlated with nutritional status—anaemia,[7] weight loss,[30] low BMI,[10 29] cachexia[11 34]—have been associated with poor survival of patients with Alzheimer's disease, but the issue remains incompletely explored.[14] In all models presented in our study, a condition of malnutrition was associated with increased mortality. We estimated nutritional status based exclusively on BMI calculation, which is not an accurate indicator of protein-calorie malnutrition that is expected to be the hallmark of these patients.[61] None the less, MDS-based BMI measures identify patients with malnutrition.[50] Malnutrition affects immune response and causes malabsorption, thus worsening nutritional status as well as reflecting the effects of the disease status. However, malnutrition is the end result of several medical and social conditions that chronically affect elderly people and it can therefore be considered a marker of frailty in demented patients.[62]

This study confirms some of the findings of previous studies, but it is at variance with others. A possible explanation for these differences may be due to the study setting. Indeed studies of patients admitted to long term care institutions may result in selective identification of those patients more severely affected by the disease. Another source of variation is the difference in the criteria used to diagnose Alzheimer's disease.[63] In the present study, the diagnosis was confirmed on review of hospital discharge record documentation and was likely consistent with the criteria for the clinical diagnosis of probable Alzheimer's disease developed by the NINCDS-ADRDA working group. In a nursing home study similar to ours, a panel of experts reviewing clinically relevant information confirmed in nearly 80% of cases the diagnosis made by lay evaluators.[64] In our study the diagnosis was made clinically and we lack any pathological data. However, severe fallacies have been reported in the pathological confirmation of the diagnosis of Alzheimer's disease.[65 66] Finally, criteria used to screen dementia severity, performance in physical function, and the definition of factors tested as predictors have also varied widely in previous studies.

Some limitations of the present study should be considered. Although patients were drawn from a broad geographic area in the United States and had standardised and validated assessment, they are not necessarily representative of all patients affected by Alzheimer's disease. However, with respect to the generalisability of our results, or lack thereof, van DjiK *et al*[7] found very similar findings among 606 demented patients admitted to a Dutch nursing home facility. Moreover, our focus has been on prevalent and not on incident cases of Alzheimer's disease. As the use of prevalent cases tends to exclude those with rapidly progressive disease and short survival, we cannot exclude that selective survival explains all or part of the results found. However, it is likely that this results in an underestimation of the effect of the disease on mortality. The analytical strategy adopted is not devoid of potential pitfalls. Although we studied predictors using a longitudinal approach, information was gathered at initial MDS assessment, impeding the examination of time dependent predictors. False associations between mortality and baseline variables could have occurred by chance owing to the analysis of several variables. For

this reason we included only a subset of variables selected a priori from a larger set of MDS data. We based the selection on the findings of previous studies, and on the likelihood that a variable might affect survival. Furthermore, future studies would have to investigate whether and how the effect of medical factors on mortality varies according to sociodemographic variables. Despite a large cohort of patients, we may have had insufficient power to detect a true difference with some variables that were uncommon in this population (aphasia). Finally, as we assessed whether predictors differed by cognitive impairment without a formal test for interaction, independence cannot be ascertained conclusively.

In conclusion, this study expands our knowledge of the prognostic determinants in patients living in nursing homes and provides useful information about the clinical course of Alzheimer's disease. Although there are many risk factors for mortality in this elderly population, the factors with the strongest association with mortality seem to be those with the greatest potential for modification. For caregivers, these results suggest that efforts should be made to minimise these factors. A "high-tech" intervention would hardly ever be justifiable; likewise a "nihilistic" approach is not appropriate.[67] Intervention aimed at improving physical conditioning, optimising function in activities of daily living, considering malnutrition, and preventing pressure sores should be considered as they may considerably improve the quality of life of demented patients. Further studies will also have to clarify discordant results about the impact of some of these intervention programmes on functional wellbeing and survival.[68–70]

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