

## Research Article

# Cognitive Aging Trajectories and Burdens of Disability, Hospitalization and Nursing Home Admission Among Community-living Older Persons

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## Abstract

**Background.** The course of cognitive aging has demonstrated substantial heterogeneity. This study attempted to identify distinctive cognitive trajectories and examine their relationship with burdens of disability, hospitalization, and nursing home admission.

**Methods.** Seven hundred and fifty-four community-living persons aged 70 years or older in the Yale Precipitating Events Project were assessed with the Mini-Mental State Examination every 18 months for up to 108 months. A group-based trajectory model was used to determine cognitive aging trajectories while adjusting for age, sex, and education. Cumulative burden of disabilities, hospitalizations, and nursing home admissions over 141 months associated with the cognitive trajectories were evaluated using a generalized estimating equation Poisson model.

**Results.** Five distinct cognitive trajectories were identified, with about a third of participants starting with high baseline cognitive function and demonstrating *No decline* during the follow-up period. The remaining participants diverged with *Minimal* (prevalence 41%), *Moderate* (16%), *Progressive* (8%), and *Rapid* (3%) cognitive decline. Participants with *No decline* incurred the lowest incidence rates (per 1,000 person-months) of disability in activities of daily living (ADL; 75, 95% confidence intervals: 60–95) and instrumental ADL (492, 453–535), hospitalization (29, 26–33) and nursing home admission (18, 12–27), whereas participants on the *Rapid* trajectory experienced the greatest burden of ADL disability (612, 595–758) and those on the *Progressive* trajectory had the highest nursing home admission (363, 292–451).

**Conclusions.** Community-living older persons follow distinct cognitive aging trajectories and experience increasing burdens of disability, hospitalization, and nursing home placement as they age, with greater burdens for those on a declining cognitive trajectory.

**Keywords:** Cognitive aging trajectories—Mini-Mental State Examination—Functional disability—Hospitalization—Nursing home admission

Increases in life expectancy have led to rapid population aging worldwide, along with an unprecedented “dementia epidemic” (1). In the United States, more than 13.9% of adults older than 70 years have some form of dementia (1,2). Another 22% have cognitive impairment or precursor brain changes implicated in Alzheimer’s disease (AD), the most common neurodegenerative dementia (1–3). Older persons with dementia have an increased risk of functional dependence, death (4,5), hospitalization (5,6), and institutionalization (5,7), and hence, poses tremendous burdens on the health care systems, patients, their families, and society.

However, early detection of AD and dementia is hampered by the heterogeneity in the natural course of the disease (8–12). Both the rate of cognitive decline (9–11) and the change point at which the cognitive deterioration accelerates (10) vary across populations and show an overlap with mild cognitive impairment without dementia and “normal” cognitive aging (10–12). Neuropathological markers typical of AD are found in the brains of older persons with normal cognitive function (12). These observations raise the possibility that cognitive aging may encompass a continuum of biological brain changes, with phenotypes ranging

from optimal cognitive function to neurodegenerative dementia (11–13), possibly through genetically determined developmental mechanisms (13,14) or cumulative environmental exposure (15). Therefore, elucidating cognitive aging heterogeneity from population continuum perspective may help identify characteristics associated with progressive cognitive deterioration and develop a holistic interventional strategy to reduce burden of cognitive impairment and dementia (4–7).

Small and colleagues (16) applied a growth mixture model to a cohort of 528 Swedish elders aged 80 years or older. Based on the Mini-Mental State Examination (MMSE) scores assessed on three occasions over 7 years, two latent classes were mapped to corresponding clinical diagnostic groups, AD versus dementia free. Another study followed 2,043 elders in U.K. over four occasions using the MMSE (17). Based on a growth mixture model, three patterns of cognitive change were identified as slow (41%), accelerating (54%), and steep constant (5%) decline (17). A similar finding of three latent classes of slow (65%), moderate (27%), and fast (8%) decline was reported from 1,049 elderly clergy based on a composite cognitive score (18). However, these studies may not fully reveal cognitive aging heterogeneity due to restriction on the number of latent classes (16,17). In addition, they have not related cognitive trajectories to functional disability and patterns of health care utilizations. Given the emerging literatures on the relationship between “normal” cognitive aging and risks of functional decline, mortality, hospitalization (4,5,19) and possibly, nursing home admissions (5,7), elucidating whether these relationships vary across different trajectories of cognitive aging is of great public health interest.

We sought to identify distinctive cognitive trajectories among initially nondisabled community-living elders using longitudinal data on a global cognitive test. With an unparalleled data source with monthly assessments of functional disability and health care utilizations between waves of cognitive assessments (20–22), we examined clinical and public health implications of the cognitive aging trajectories. We hypothesized that the course of cognitive aging is heterogeneous yet could be phenotypically represented by distinctive trajectories. Moreover, these cognitive aging phenotypes should demonstrate a gradient pattern of functional disability, hospitalization, and nursing home admission consistent with the magnitude of cognitive decline.

## Methods

### Study Population

The Yale Precipitating Events Project is a longitudinal study of 754 community-living persons aged 70 years or older, assembled between March 1998 and October 1999. All participants were nondisabled at baseline, requiring no personal assistance with four basic activities of daily living (ADL) tasks—bathing, dressing, walking inside the house, and transferring from a chair (20,21). The study protocol was approved by the Yale Human Investigation Committee. Complete details about the sampling frame and inclusion/exclusion criteria have been described previously (20,21). The current study used data collected through December 31, 2009, with home-based comprehensive assessments completed every 18 months for 108 months and monthly telephone interviews completed up to 141 months (22). The completion rates for the home-based assessments were 100% at baseline and >95% during the follow-up. Of the participants, 433 (57.4%) died after a median survival of 56.5 months, and 35 (4.6%) dropped out of the study after a median follow-up of 23.5 months.

## Study Measurements

### Cognitive function

Cognitive function was assessed by a trained research nurse at baseline and then every 18 months during the comprehensive assessments using the MMSE (23). The MMSE is the most widely used instrument for screening cognitive impairment and assessing global cognitive function in both clinical and research settings, with higher scores indicating better performance (range: 0–30). Studies of its psychometric properties show moderate-to-high levels of short-term test–retest reliability, construct and criterion validity, and adequate responsiveness to cognitive change over time (8,24,25).

### Covariates of cognitive aging

During the comprehensive assessments, we collected data on demographic characteristics (age, sex, race, living condition, and education) at baseline and nine self-reported, physician-diagnosed chronic conditions (hypertension, myocardial infarction, congestive heart failure, stroke, diabetes mellitus, arthritis, hip fracture, chronic lung disease, and cancer) (20–22), and depression symptoms using the short-form of the Center for Epidemiologic Studies–Depression scale (CES-D) (26), at baseline and then every 18 months.

### Functional disabilities, hospitalizations, and nursing home admissions

During monthly telephone interviews, we asked participants, “At the present time, do you need help from another person to (complete)?” bathe, dress, walk inside the house, and transfer from a chair. Those who needed help with any of these four tasks were considered “disabled” at that given month with basic ADL function. Instrumental ADL (IADL) was assessed in a similar fashion based on five tasks: shopping, doing housework, preparing meal, taking medications, and managing finance. The reliability of these assessments was high, with  $\kappa$  ranging from 0.75 to 1.0 (20–22). Participants were also asked, during the previous month, whether they had stayed overnight in a hospital ( $\kappa = 0.94$ ) (20–22) and whether they had been admitted to and currently stayed in a nursing home ( $\kappa = 0.96$ ) (21). Although hospitalizations mostly result from acute medical conditions or physical injuries, nursing home placement usually indicates marked deterioration in both physical health and functional capacities often seen in advanced dementia (5,7).

## Statistical Analyses

The baseline characteristics of the study cohort were summarized using means ( $\pm SD$ ) or frequency (percentages) and compared across cognitive aging trajectories using the Chi-square test and the Cochran–Armitage linear trend test, as appropriate.

To identify distinct trajectories of cognitive aging, we used group-based trajectory modeling with the SAS macro Proc Traj (27,28), which fits a semiparametric (discrete) mixture model to longitudinal data using the maximum likelihood function, without random effects. The MMSE scores from the 18-month comprehensive assessments were modeled as a censored normal distribution, with each participant contributing one to seven observations (Mean  $\pm SD$ :  $5.2 \pm 2.1$ ).

To determine an optimal number of trajectories, we screened alternative models of one to eight groups with slope parameters varying through linear, quadratic, and cubic terms using the Bayesian Information Criterion (BIC) (27–29). We then included the main effects for three a priori selected demographic factors, age (in years),

sex (men vs women), and education less than 12 years as predictors of group membership probabilities, given their established role in determining the level or speed of cognitive aging or course of dementia (8–10,15–19). We assessed model adequacy using the average posterior probability of assignment, proportion of group membership with a posterior probability of assignment less than 70%, and the differences between the predicted group probability and observed group proportions (28). We selected the final model using the aforementioned diagnostics, plus practical considerations of distinctiveness and interpretability of the estimated trajectories (28,29), including a minimum group size of 2.5%. Ninety-five percent confidence intervals (95% CI) for group proportions were empirically derived using 1,000 bootstrapped samples.

We used generalized estimating equations (30) Poisson models to examine the relationship between the cognitive trajectories and cumulative burdens of functional disability, hospitalization, and nursing home admission during the 141-month follow-up period. To quantify cumulative burden, we estimated incidence density rates and their 95% CI as total number of events per 1,000 person-months based on monthly telephone interviews across seven 18-month intervals, using separate models for different outcomes. An “event” occurred when participants reported an ADL or IADL disability, hospitalization, or nursing home admission for a given month. In these models, the cognitive trajectories were represented by dummy indicators. Global model fit was checked using the Quasi-likelihood Information Criterion. Next, we compared the cumulative burdens across cognitive trajectories after adjusting for age, sex, education, depression symptoms, and number of chronic conditions. These factors may potentially confound an observed relationship with cognitive trajectories. In addition, we explored the “time course” of these cumulative burdens by including cognitive trajectories by years of assessment interactions, to derive average annual percent increments (or decrements) of the interval-specific incidence rates from the first to the last 18-month intervals for each trajectory group. Finally, we examined cumulative mortality for each trajectory.

We performed sensitivity analyses to assess the robustness of the final trajectory model. First, we refit the model by including CES-D scores and number of chronic conditions as time-varying covariates of each cognitive trajectory. Second, we restricted the analyses to participants with three or more assessments. Third, we excluded participants with a baseline MMSE score of less than 24, indicative of potential cognitive impairment (21–4). Finally, to provide clinical insights, we identified potential cases of AD and other dementias among decedents based on the immediate or underlying causes of death with an ICD-10 (International Classification of Diseases, 10th Revision) code of F03, G30.0–G30.9, and R54 (20) on death certificates, recognizing that these conditions are often underreported.

All the statistical analyses were conducted using SAS software version 9.3 (SAS Institute, Cary, NC). The hypotheses were tested at a two-sided significance level of  $\alpha = .05$ .

## Results

### Characteristics of Study Population

At baseline, the 754 participants had an average age of 78 ( $\pm 5.3$ ) years and 12 years of education ( $\pm 2.9$ ), with the majority being women (64.6%), White (90.5%), living with others (60.5%), and having  $\leq 2$  chronic conditions (53.7%). About 11% and 13% of participants had potential cognitive impairment or depressive symptoms (Table 1).

### Estimated Cognitive Aging Trajectories

Among the trajectory models screened, a five-group solution (BIC:  $-9,449$ ) adjusted for the three predefined risk factors (age, sex, and education) was selected as the final model because of its high BIC and better discrimination than the model with the highest BIC (Supplementary Material: Table 1, Table 2, and text). The maximum likelihood estimates for the final five-group trajectory model are summarized in Table 2. The 754 participants demonstrated diverging cognitive trajectories, with 32.5% (95% CI: 21.4–43.6%) showing *No decline*, whereas the others following a path of *Minimal* (40.6%, 32.4–52.2%), *Moderate* (16.6%, 9.1–19.1%), *Progressive* (8.4%, 4.2–12.3%), and *Rapid* (2.8%, 1.2–5.3%) decline, respectively.

The predicted and observed cognitive trajectories are presented in Figure 1.

### Risk Factor Profiles of Cognitive Aging Trajectories

The risk factor profiles for the trajectories are presented in Supplementary Table 3. All factors, except chronic conditions ( $\chi^2$  test,  $df = 4$ ,  $p = .07$ ), differed across the trajectories ( $\chi^2$  test,  $df = 4$ ,  $p = .04$  to  $<.001$ ).

### Cumulative Burdens of Disability, Hospitalization, and Nursing Home Admission by Cognitive Aging Trajectory

The cumulative burdens of disability, hospitalization, and nursing home admission during the follow-up period by trajectory groups are provided in Table 3. The *No decline* group had the lowest burden, whereas the *Progressive* and *Rapid decline* groups had the highest. After adjusting for covariates, the four declining trajectories had significantly higher burdens than the *No decline* trajectory (see Supplementary Material for details).

Over seven successive 18-month intervals, the average annual percentage increment of interval-specific incidence rates of ADL disabilities were 29% for the *No decline*, 32% for *Minimal decline*, 39% for *Moderate decline*, 26% for *Progressive decline*, and 33% for *Rapid decline* trajectory. The corresponding estimates were 11%, 11%, 8%, 7%, and 7% for IADL disability and 49%, 47%, 55%, 39%, and 33% for nursing home admissions ( $p$  values for

**Table 1.** Characteristic of the Study Cohort at Baseline ( $N = 754$ )

Age (y), mean $\pm$ SD	78.4 $\pm$ 5.3
$\geq 85$ , $n$ (%)	102 (13.5)
Female, $n$ (%)	487 (64.6)
Non-White race, $n$ (%)	72 (9.5)
Living alone, $n$ (%)	298 (39.5)
Education (y), mean $\pm$ SD	12.0 $\pm$ 2.9
$<12$ y, $n$ (%)	249 (33.0)
No. of chronic conditions,* mean $\pm$ SD	1.8 $\pm$ 1.2
$\geq 2$ , $n$ (%)	405 (53.7)
CES-D score, <sup>†</sup> mean $\pm$ SD	9.0 $\pm$ 8.6
$\geq 20$ , $n$ (%)	100 (13.3)
MMSE score, <sup>‡</sup> mean $\pm$ SD	26.8 $\pm$ 2.5
$<24$ , $n$ (%)	86 (11.4)

Notes: CES-D = Center for Epidemiologic Studies Depression scale; MMSE = Mini-Mental State Examination; SD = standard deviation.

\*Based on nine self-reported, physician-diagnosed conditions, including hypertension, myocardial infarction, heart failure, stroke, diabetes mellitus, arthritis, hip fracture, chronic lung disease, and cancer.

<sup>†</sup>Sex-adjusted score on the CES-D, range: 0 to 60.

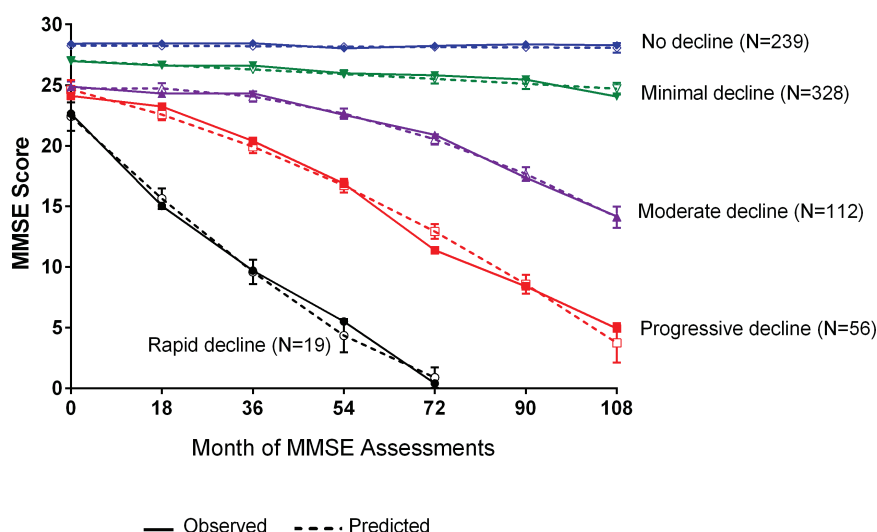
<sup>‡</sup>Range: 0–30.

**Table 2.** The Final Five-group Trajectory Model of MMSE Scores Among 754 Community-living Older Persons

Trajectory Group	Predicted Group Probability	Growth Parameter	Maximum Likelihood Estimates*		
			Est.	SE	p Value
No decline	32.5	Intercept	28.80	0.15	<.001
		Linear	−0.03	0.03	.241
Minimal decline	40.6	Intercept	27.20	0.13	<.001
		Linear	−0.27	0.03	<.001
Moderate decline	15.6	Intercept	24.72	0.27	<.001
		Linear	0.26	0.14	.062
		Quadratic	−0.16	0.02	<.001
Progressive decline	8.4	Intercept	24.65	0.34	<.001
		Linear	−1.20	0.20	<.001
		Quadratic	−0.13	0.02	<.001
Rapid decline	2.8	Intercept	22.41	0.59	<.001
		Linear	−4.76	0.56	<.001
		Quadratic	0.16	0.10	.115

Notes: Est. = parameter estimate; MMSE = Mini-Mental State Examination; SE = standard error of parameter estimate.

\*Adjusted for three baseline risk factors, including age, sex, and education <12 years (see [Supplementary Material](#) for details).



**Figure 1.** Cognitive aging trajectories over 108 months among 754 community-living older persons. Mini-Mental State Examination (MMSE) scores on y-axis range from 0 (worst) to 30 (best). The solid lines depict the observed trajectories. The dotted lines depict the predicted trajectories, with I bars representing 95% confidence intervals.

interactions ranging from .03 to <.001), respectively. For hospitalization, the average annual percentage increments were 5% ( $p = .047$ ) for the *No decline* and 8% for the *Minimal* ( $p = .001$ ) and *Moderate* ( $p < .001$ ) decline; no significant linear trend was detected for the *Progressive* ( $p = .72$ ) and *Rapid* ( $p = .12$ ) decline groups.

The observed incidence rates during each 18-month interval are presented in [Supplementary Figure 1](#). Consistent with the aforementioned model-predicted time trend, these interval-specific rates tended to increase over time for all cognitive trajectories, except for the hospitalization rates. The latter seemed to fluctuate over time for the *Progressive decline* and incurred an abrupt increase during 72–89 months for the *Rapid decline*.

### Cumulative Mortality According to Cognitive Aging Trajectories

The cumulative mortality over 141 months were 37.2% ( $n = 89$ ) for *No decline*, 60.1% ( $n = 197$ ) for *Minimal decline*, 73.2% ( $n = 82$ ) for *Moderate decline*, 82.1% ( $n = 46$ ) for *Progressive decline*, and

100.0% ( $n = 19$ ) for *Rapid decline* ( $\chi^2$  test,  $df = 4$ ,  $p < .001$ ), with a gradient increment from the *No decline* to the *Rapid decline* trajectories (Cochran–Armitage trend test,  $df = 1$ ,  $p < .001$ ).

### Sensitivity Analyses

When introducing the time-varying depression symptoms and chronic conditions into the final trajectory model, or restricting the analyses to those with three or more cognitive assessments ( $n = 690$ ), neither the shapes nor the estimated group probabilities changed materially. After excluding 86 participants with potential cognitive impairment (ie, MMSE < 24), the shapes of trajectories were largely maintained, whereas group proportions changed most appreciably for the *No decline* (from 32.5% to 36.9%), *Progressive* (from 8.4% to 5.3%), and *Rapid* (from 2.8% to 1.4%) decline groups. Among the 433 decedents, the prevalence of potential dementia corresponding to the five trajectories were 4.5%, 9.1%, 28.1%, 34.8%, and 47.4%, with a gradient increment from the *No decline* to the *Rapid decline* (Cochran–Armitage linear trend test,  $df = 1$ ,  $p \leq .001$ ).

**Table 3.** Cumulative Burdens of Disability, Hospitalization, and Nursing Home Admission During the Follow-up Period According to Cognitive Aging Trajectories

Trajectory Group*	Participants	ADL Disability	IADL Disability	Hospitalization	Nursing Home Admission
No decline	239	75.1 (59.5, 94.9)	492.4 (452.9, 535.3)	29.1 (25.7, 33.0)	17.6 (11.6, 26.8)
Minimal decline	328	199.3 (171.7, 231.3)	614.6 (577.7, 654.0)	46.2 (41.8, 51.0)	56.1 (43.6, 72.2)
Moderate decline	112	338.4 (289.5, 395.4)	811.7 (776.9, 848.1)	53.9 (47.6, 60.9)	153.8 (116.8, 202.6)
Progressive decline	56	575.9 (517.5, 640.8)	878.5 (850.3, 907.6)	52.9 (43.3, 64.5)	363.5 (293.3, 450.5)
Rapid decline	19	612.4 (494.9, 757.8)	864.6 (783.7, 953.8)	43.2 (29.8, 62.6)	312.1 (174.3, 558.7)

Notes: ADL = activities of daily living; IADL = instrumental activities of daily living.

Values represent predicted number of events (95% confidence intervals) per 1,000 person-months based on separate generalized estimating equation Poisson models for each outcome.

\*Estimated using a five-group trajectory model of the Mini-Mental State Examination scores over seven assessments, adjusting for age, sex, and education.

## Discussion

Among this community-dwelling cohort of older adults followed more than 11 years, we identified five distinct cognitive trajectories based on longitudinal assessment of global cognitive function. A minority (33%) of participants maintained high level of cognitive function throughout the follow-up period; whereas the others demonstrated diverging paths of *Minimal* (41%), *Moderate* (16%), *Progressive* (8%), and *Rapid* (3%) cognitive decline. Risk factor profiles, cumulative burdens of disability, and nursing home admission closely tracked the cognitive trajectories, with the most favorable ones (ie, *No decline* and *Minimal decline*) experiencing the lowest burden and the least favorable ones (ie, *Progressive* and *Rapid decline*) experiencing the highest. These findings support that cognitive aging is a heterogeneous process, consisting of multiple latent developmental trajectories, rather than following a homogeneous average trajectory (10,11,16–18).

Our findings are consistent with previous studies; for example, a rapid decline trajectory emerged from Terrera and colleagues (17) and Hayden and colleagues (18). Similarly, our minimum decline trajectory is comparable with the slow decline in Terrera's study (17) in terms of group prevalence (41%) and linear slope. The consistent observations across studies highlight their importance as potential "phenotypes" of cognitive aging. However, our study extended previous studies in important ways. First, we identified a trajectory without appreciable cognitive decline, which may represent a phenotype consistent with the conceptual model for "successful aging" (31) and the empirical evidence for optimal functional aging (22,32,33). Second, we identified a progressive trajectory with moderate yet accelerated rate of decline and a relatively uncommon trajectory of precipitous deterioration. These two least favorable cognitive trajectories had the most risk factors, experienced the greatest overall burdens of disabilities and nursing home admissions and collectively accounted for 82% of the dementia cases among decedents. These attributes are consistent with a preclinical course of AD and suggest that these two trajectories may serve as potential prototypes for probing "dementia phenotypes" (4,6–8,10–12,16).

Conversely, we found that the cumulative burden of hospitalization and its "time course" did not track worsening cognitive trajectory as closely as the functional disability or nursing home admission did, especially in the two least favorable trajectories, suggesting that the risk of hospitalization may vary across subpopulations of cognitive aging rather than uniformly increasing with cognitive decline (5–7,19). It is beyond the scope of this study to ascertain whether this observation may reveal diverse patterns or pathways toward hospital versus nursing home care during the course of cognitive aging, or merely depicted a "healthy survivor" phenomenon.

This study has strengths, as well as limitations. Unlike studies that relied on external, claim-based data and infrequent follow-up assessments (5–7,16–19), we ascertained functional disabilities, hospitalizations, and nursing home admissions via monthly telephone interviews coupled with review of medical records and death certificates. Furthermore, we tracked indicators of human aging beyond the cognitive domain, which allowed external validation of the cognitive aging trajectories in clinical and public health context. Admittedly, the MMSE, like other brief cognitive tests, has been criticized for floor/ceiling effects, insensitivity to small cognitive changes, and omitting executive ability (8,16,24,25,33). Use of group-based trajectory modeling might partially circumvent such limitations via dissecting a heterogeneous population-average into relatively homogeneous subtrajectories, yet the lack of random effects may lead to over-estimating the number of classes (29). The proximity of the minimal decline to the no decline trajectories may echo this "trade-off," despite their appreciable separation with regard to cumulative burdens of disabilities, hospitalizations, and nursing home admissions. Finally, study participants were members of a single health plan and may not be representative of elders in other settings.

To conclude, we identified five distinct cognitive trajectories and documented their close relationships with risk factors and the burdens of disability, nursing home placement, and mortality over the course of cognitive aging. These findings provide empirical evidence for the validity of the estimated cognitive trajectories as potential cognitive aging phenotypes. The increasing burden of disability, hospitalizations, and nursing home placements over time across the cognitive trajectories suggests that most elders face the challenges of biological aging. Future studies incorporating domain-specific cognitive measures, patient-level random effects, and reasons for hospitalization are warranted.

## Supplementary Material

Please visit the article online at <http://gerontologist.oxfordjournals.org/> to view supplementary material.

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