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Predictors That a Diagnosis of Mild Cognitive Impairment Will Remain Stable 3 Years Later

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Abstract

Background and Objective—In half to two thirds of patients who are diagnosed with mild cognitive impairment (MCI), the diagnosis neither converts to dementia nor reverts to normal cognition; however, little is known about predictors of MCI stability. Our study aimed to identify those predictors.

Methods—We obtained 3-year longitudinal data from the National Alzheimer's Coordinating Center Uniform Data Set for patients with a baseline diagnosis of MCI. To predict MCI stability, we used the patients' baseline data to conduct three logistic regression models: demographics, global function, and neuropsychological performance.

Results—Our final sample had 1,059 patients. At the end of 3 years, 596 still had MCI and 463 had converted to dementia. The most reliable predictors of stable MCI were higher baseline scores on delayed recall, processing speed, and global function; younger age; and especially the absence of *ApoE4* alleles.

Conclusions—Not all patients with MCI progress to dementia. Of the protective factors that we identified from demographic, functional, and cognitive data, the absence of *ApoE4* alleles best predicted MCI stability. Our predictors may help clinicians better evaluate and treat patients, and may help researchers recruit more homogeneous samples for clinical trials.

Keywords

mild cognitive impairment; dementia; *ApoE4*; cognitive; Alzheimer disease

Alzheimer disease (AD) is a progressive, fatal neurodegenerative disease with a median time from diagnosis to death of about 7 to 10 years (Todd et al, 2013). The “pathogenic cascade” of AD is thought to begin 10 to 20 years before patients show their first symptoms of cognitive impairment (Hardy and Selkoe, 2002). For carriers of the apolipoprotein E4 (*ApoE4*) allele, brain alterations associated with AD may begin as early as infancy (Dean et al, 2014).

Mild cognitive impairment (MCI) is a diagnostic category thought to represent an intermediate level of functional and cognitive decline between normal aging and dementia (Petersen, 2004). Historically, MCI has been considered prodromal AD (Petersen, 2004); in patients who go on to develop AD, symptoms appear on average within 2 to 3 years (Lopez et al, 2012). Patients with MCI develop AD or another form of dementia at a rate of about 10% per year (Ganguli et al, 2004; Lopez et al, 2012; Mitchell and Shiri-Feshki, 2009; Petersen et al, 1999).

The literature has supported the use of demographic, genetic/medical, and cognitive markers to identify the patients with MCI who are at highest risk of converting to AD. Shown to be at highest risk are older people, women, carriers of *ApoE4*, and people with fewer years of education, lower scores on the Mini-Mental State Examination (MMSE), vascular disease, and late-life depression (Akinyemi et al, 2013; Li et al, 2016; McClintock et al, 2010; Purnell et al, 2009).

Similar studies have examined patients who revert from MCI to normal or near-normal cognition. In a large nationally representative clinic-based cohort, about 16% of patients reverted to normal cognition over 1 year; the best predictors of reversion were fewer functional impairments, higher global function, and absence of *ApoE4* alleles (Koepsell and Monsell, 2012). Unfortunately, reverts remain at high risk of progressing to dementia within 3 years (Koepsell and Monsell, 2012). Oscillating between diagnostic categories can be associated with medical and psychiatric comorbidities (Grande et al, 2016). Thus, it appears that MCI reversion does not indicate diagnostic stability, and likely represents a heterogeneous group of disorders.

Despite our substantial understanding of MCI converters, little is known about the 47% to 67% (Ganguli et al, 2004; Lopez et al, 2012; Peters et al, 2014; Sachdev et al, 2012) of patients diagnosed with MCI who neither revert to normal cognition nor convert to dementia. Even in a large community sample, 10 years after a diagnosis of MCI, 21% of those expected to be at highest risk for converting to dementia (Dubois and Albert, 2004; Jicha et al, 2006) maintained a diagnosis of MCI (Ganguli et al, 2004). This finding suggests that certain individuals may not convert to AD, but instead remain diagnostically stable over time.

While a great many studies have characterized patients who convert from MCI to dementia, surprisingly few have systematically characterized patients whose MCI remains stable. Many studies have used MCI-stable participants as a reference group in modeling conversion to dementia (Li et al, 2014; van Rossum et al, 2012) or reversion to normal cognition (Tokuchi et al, 2014). Some researchers who were modeling conversion to dementia grouped MCI-stable participants with participants who had reverted to normal cognition, while other researchers, modeling reversion to normal cognition, grouped MCI-stable participants with converters (Jefferson et al, 2015; Kim et al, 2013). These heterogeneous groups were likely created to increase sample size, but such methods lead to imprecise conclusions about factors that predict MCI stability. Individuals who remain stable over time may have unique and distinct clinical characteristics, and efforts to explore this group have been underrepresented.

The aim of our current study was to address this gap in the literature by identifying predictors of an MCI diagnosis remaining stable over time. We compared patients with stable MCI to patients who had converted to dementia, and we analyzed the influence of demographic, neuropsychological, and functional factors. We hypothesized that younger age, male sex, higher education level, fewer *ApoE4* alleles, intact global and adaptive function skills, and better neuropsychological performance would distinguish those whose diagnosis at 3 years remained MCI.

METHODS

Participants

Data for this retrospective 3-year study were collected between September 2005 and July 2013 from 34 then-current US Alzheimer's Disease Centers as part of the National Alzheimer's Coordinating Center (NACC) Uniform Data Set (Beekly et al, 2007; Morris et al, 2006). Our inclusion criteria were:

- MCI diagnosis (by a single clinician or by consensus of two or more clinicians) at the baseline visit, using standard criteria (Petersen and Morris, 2005)
- Completion of demographic information and measures of global and neuropsychological function at the baseline visit
- Completion of three annual on-site follow-up visits, each within 18 months of the previous visit; at each visit, the patients were again given a diagnosis and their demographic information and measures of global and neuropsychological function were repeated

We designated participants as being *MCI-stable* if their diagnosis at all three follow-up visits was still MCI, regardless of MCI subtype. We designated participants as *MCI converters* if they had a dementia diagnosis at both the 2- and 3-year follow-up visits, regardless of the diagnosis at 1-year follow-up. We considered those who were reported to have normal cognition at both 2- and 3-year follow-up as *MCI reverters*.

A total of 1,778 participants met our inclusion criteria for the study. At 3-year follow-up, 596 (34%) still had a diagnosis of MCI, 463 (26%) had converted to dementia, 461 (26%)

had reverted to normal cognition, and 258 (14%) were categorized as *impaired/not MCI*, defined by the NACC as cognitive impairment that neither fully meets MCI criteria nor represents normal aging (Beekly et al, 2004).

Since our sole focus in this study was to identify baseline predictors of maintaining a diagnosis of MCI over 3 years, we excluded from the study all participants who had reverted to normal cognition or were categorized as impaired/not MCI at 2 and/or 3 years. This exclusion reduced within-group variability and isolated the MCI-stable patients so that we could analyze predictive factors that might have differentiated them from converters.

Our final sample had 1059 participants. Table 1 lists baseline demographic characteristics, baseline global function, and MCI subtypes for the overall sample and the two subgroups. Table 2 presents the baseline neuropsychological test scores for the full sample and the subgroups.

Procedure

We pulled the following data from the NACC Uniform Data Set: demographic information, clinicians' neurocognitive diagnoses (including MCI subtypes), global function, neuropsychological performance, and genetic data for all available visits. Although some patients had data for up to nine annual follow-up visits (mean = 3.29 years, standard deviation = 1.90), we chose to examine follow-up data for just 3 years to maintain adequate sample sizes in both groups.

We analyzed the following variables:

Demographics: Age, sex, education level, ethnicity (Hispanic or non-Hispanic), MCI subtype (amnesic or nonamnesic), *ApoE4* alleles (no copies, 1 copy, or 2 copies), vascular burden (sum of cardiovascular risk factors and related medical conditions), and self-reported depression in the past 2 years or clinician-diagnosed depression at baseline.

Global function: Functional Activities Questionnaire total scores (assessing functional impairment relative to previous abilities), MMSE (a cognitive screen; scores were demographically corrected [Shirk et al, 2011]), and Clinical Dementia Rating Scale–Sum of Boxes (CDR–SUM, assessing the severity of functional impairment). For details on the tests, see Weintraub et al, 2009.

Neuropsychological performance: Scores on measures assessing the cognitive domains of attention, memory, information processing speed, executive function, and language: the Wechsler Memory Scale-Revised, Digit Span Forward and Backward, Wechsler Memory Scale-Revised Logical Memory (Story A) Immediate and Delayed Recall, Wechsler Adult Intelligence Scale-Revised Digit Symbol, Trail Making Test Parts A and B, Animal Fluency, Vegetable Fluency, and Boston Naming Test (30 items). Again, for details on the tests, see Weintraub et al, 2009. We corrected the scores for age, sex, and education, and transformed them into *z*-scores using published norms (Shirk et al, 2011).

Statistical Analysis

We conducted univariate analyses on the baseline differences between the MCI-stable and conversion groups on measures gathered at participants' initial (baseline) visit. We performed independent samples *t* tests on demographic factors, baseline scores on measures of global function, and baseline neuropsychological performance. We used nonparametric Mann-Whitney *U* tests in lieu of independent samples *t* tests when analyzing group differences on variables with non-normal distributions. We used chi-square tests for between-group analyses of sex, ethnicity, depression, vascular burden, diagnostician (single clinician or consensus), and number of *ApoE4* copies.

Because of our large sample size and the likelihood of detecting significant differences, we calculated effect sizes for all univariate tests. According to Cohen (1988), effect sizes of 0.20, 0.50, and 0.80 indicate small, moderate, and large effects, respectively. We excluded variables from regression analyses if they had significant univariate group differences but effect sizes well below the threshold for small effects (ie, $d < 0.1$, $r < 0.05$ [Cohen, 1988]). We entered all remaining variables into multivariable predictive models to identify the most influential predictors of MCI stability.

Because we had data on three follow-up visits for all participants, we performed predictive analyses using three separate binary stepwise logistic regression models. We performed the regression models predicting MCI-stable individuals, with MCI converters as the reference group for the three categories: demographic, global function, and neuropsychological performance.

Finally, we entered all significant predictors from each separate category-level regression model into one overall binary stepwise logistic regression model to identify the most robust predictors of MCI stability at 3 years.

We evaluated the goodness of fit of the logistic regression models using the Hosmer-Lemeshow *P* value and Area Under the Curve. The Hosmer-Lemeshow *P* value indicates how well the model fits the data. A value > 0.05 denotes sufficient model fit, and values above 0.40 denote very good fit (Tabachnik and Fidell, 1996). Area Under the Curve indicates the accuracy of a predictor or set of predictors in distinguishing categories of individuals (in this instance, stable individuals from converters). Values of 0.50 denote the flip of a coin, and 1.00 denotes a perfect prediction (Tabachnik and Fidell, 1996).

We performed all of the statistical analyses using Statistical Analysis System (SAS®) Version 9.3 (SAS Institute, Cary, North Carolina), with two-sided hypotheses tests. We set significance at $P < 0.05$. If participants were missing a particular score in a given category, we excluded them from the analysis of that category (ie, listwise deletion).

RESULTS

Univariate Analysis

Demographics—Neither sex distribution nor diagnostician was significantly different between the MCI-stable and MCI-conversion groups. However, the MCI-stable group was

younger, had fewer years of education, and had fewer copies of *ApoE4* than the conversion group (Table 1). Because of its negligible effect size, we excluded vascular burden from the multivariable analysis. All remaining demographic variables were above the effect size threshold and were entered into the predictive demographic model.

Global Function—Among the baseline scores of global function, the MCI-stable group had lower Functional Activities Questionnaire and CDR–SUM scores than the conversion group, but higher MMSE scores (Table 1). All of the global function variables had moderate to large effect sizes and were entered into the predictive global function model.

Neuropsychological Performance—The MCI-stable group had significantly higher scores across all neuropsychological tests except Digit Span Forward and Digit Span Backward (Table 2). Effect sizes indicated negligible differences for Digit Span Forward and Digit Span Backward, and so we omitted these variables from the predictive analyses. All of the other neuropsychological measures had small to large effect sizes and were entered into the predictive neuropsychological performance model.

Predictive Analysis

Table 3 shows all regression results for the three categories. The logistic regression model for demographics showed that fewer copies of *ApoE4* alleles, younger age, nonamnesic MCI subtype, no active or recent depression, and fewer years of education predicted MCI stability, with very good model fit (Tabachnick and Fidell, 1996).

In the logistic regression model for global function, lower CDR–SUM scores, higher MMSE scores, and lower Functional Activities Questionnaire scores predicted MCI stability, again with very good model fit.

In the logistic regression model for neuropsychological performance, higher scores on Logical Memory Delayed Recall, Vegetable Fluency, and Digit Symbol predicted MCI stability, with acceptable model fit.

The overall stepwise logistic regression analysis, which included only the significant predictors from the three category-level models, demonstrated good model fit. The most influential predictors of MCI stability were higher scores on Logical Memory Delayed Recall, Digit Symbol, and the MMSE, as well as younger age, fewer copies of *ApoE4* alleles, and lower scores on the CDR–SUM. The best single predictor was having no *ApoE4* alleles.

DISCUSSION

Few studies have specifically investigated baseline factors modeling the likelihood of MCI neither converting to dementia nor reverting to normal cognition. In this study, 34% of the patients diagnosed with MCI at their first visit remained stable at each of three annual follow-up visits. This incidence is largely consistent with those reported in previous studies (Ganguli et al, 2004, 2013; Koepsell and Monsell, 2012; Lopez et al, 2012; Mitchell and Shiri-Feshki, 2009; Peters et al, 2014; Sachdev et al, 2011), suggesting that a large subset of

patients continue to have a diagnosis of MCI without converting to dementia. Although reported incidences of MCI stability have been fairly consistent, few significant factors predicting an individual's likelihood of remaining stable have been modeled.

In our study, a series of predictive regression models showed several demographic, global function, and neuropsychological markers that were significantly associated with MCI stability. When we combined significant predictors for each individual category-level regression into an overall predictive model, the results distinguished individuals who were nearly three times as likely still to carry a diagnosis of MCI at 3-year follow-up. More than half of the predictors remained significant in the final multivariable logistic regression model, suggesting that indices from each category contributed to an individual's likelihood of remaining stable.

When we determined the relative importance of each predictor in the overall model, effect sizes (ie, odds ratios) indicated that *ApoE4*, CDR-SUM, and Logical Memory Delayed Recall are among the most influential markers. These findings highlight the independent contributions of genetic factors, functional abilities, and memory to MCI stability, and are generally consistent with the literature modeling conversion to dementia. Such studies have found risk factors for conversion to be *ApoE4* carriers (Caselli et al, 2007; Michaelson, 2014), poorer baseline neuropsychological test scores, and greater difficulty with daily activities (Aretouli et al, 2011; Devanand et al, 2008; Gomar et al, 2011).

To our knowledge, our study is the first that has specifically investigated predictors of maintaining an MCI diagnosis over time. While our results may not be altogether unexpected, they have the potential to aid clinicians and researchers alike in the study, treatment, and possible prevention of MCI and dementia.

Our findings can help clinicians determine the likelihood that their patient will maintain diagnostic stability over time. While some of our more influential predictors are similar to those identified by studies of conversion, risk factors for conversion such as education, sex, ethnicity, MCI subtype, and executive function (Campbell et al, 2013; Cloutier et al, 2015; Lee et al, 2012; Ye et al, 2013; Yoon et al, 2015) did not appear to be influential in predicting MCI stability in our overall predictive model. Further, we found that cardiovascular risk factors did not distinguish MCI-stable individuals from converters, indicating that vascular burden does not significantly affect MCI stability over 3 years. While we found depression to be predictive alongside other demographic factors, it was not significant when analyzed concurrently with functional and neuropsychological markers, suggesting that these other indices are more robust determinants of stability than is active or recent depression.

Community clinicians who are trying to predict the trajectory of MCI for a patient are unlikely to have a comprehensive record of the patient's demographic, global function, cognitive performance, and genetic data. Our category-level predictive models offer clinicians data on which to base predictions, and our overall models can help clinicians weigh the relative importance of the many factors. Clinicians working with patients who have a diagnosis of MCI can then give them some sense of certainty about its nature and

expected course, and can enable them to develop appropriate expectations and make needed plans.

In terms of research, our findings can inform the design and implementation of intervention trials, particularly studies aimed at preventing or delaying conversion to dementia. Such trials may detect intervention effects more successfully by using our findings to exclude participants who are more likely to remain MCI-stable and could cause false positives.

Our study has several strengths. First, the large, well-characterized sample represented all participating US Alzheimer's Disease Centers, which followed the patients longitudinally and gave them standardized assessments.

Second, we minimized within-group variability by defining MCI clearly and consistently when we selected our sample. For example, we excluded patients who fluctuated between MCI and normal cognition or from MCI to dementia and back to MCI, as well as participants who reverted to normal cognition or were diagnosed as impaired/not MCI. Our homogeneous sample let us draw conclusions about the influence of certain predictive factors that might apply to a typically heterogeneous population.

Third, we took a statistically conservative approach in performing the predictive analyses. Transforming cognitive scores based on normative data served to limit the impact of demographic factors on neuropsychological performance without having to account for these confounds in the predictive models. Using effect sizes at the univariate level was a parsimonious method of considering factors for entry into the predictive model. Likely as a result of these conservative approaches, effect sizes in the overall model were modest; however, model-fit indices for all regression models were well above acceptable limits and indicated well-fitting predictive models (Tabachnick and Fidell, 1996).

Our study also has limitations. Because we analyzed only 3 years' worth of follow-up data so as to maintain a large sample size, we may have identified only factors that distinguish patients with stable MCI from fast converters. Many patients have been found to convert from MCI to dementia during the first 3 to 5 years of follow-up (Devanand et al, 2008; Mitchell and Shiri-Feshki, 2009; Petersen, 2007; Petersen et al, 2005). A prospective longitudinal study with longer follow-up would let us evaluate how well our predictors generalized in a comparison of MCI-stable individuals to slower converters.

Because our participants were drawn from clinic-based populations, our results may not generalize to community populations. Our clinic-based sample may also account for our somewhat lower overall incidence of MCI-stable patients than has generally been reported in the literature, although, as noted earlier, our rate is fairly consistent with other clinic- and community-based studies.

Different NACC sites varied in whether patients were diagnosed with MCI by a single clinician or by consensus among two or more clinicians, but our results indicated no significant group differences on this factor.

While our participants demonstrated sufficient variability in sex, age, and education, the sample was not ethnically diverse.

Finally, while we strengthened our predictive analyses by excluding individuals who reverted, were diagnosed as impaired/not MCI, or oscillated between diagnostic categories, populations with these diagnoses are also worthy of study (Pandya et al, 2016).

In this initial study of factors involved in stability of MCI, we found the most protective factors to be higher scores on delayed recall, processing speed, and the MMSE, as well as younger age, fewer copies of *ApoE4* alleles, and lower scores on the CDR-SUM. Future studies of MCI stability should examine historical factors that may affect neurocognitive function, such as a history of head injury (Li et al, 2016) and medication use (Cai et al, 2013). Also valuable would be modeling stability in relation to reversion and exploring the protective quality of *ApoE2* alleles (Rebeck et al, 2002) on MCI-stable individuals.

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Glossary

AD	Alzheimer disease
<i>ApoE4</i>	apolipoprotein E4
CDR–SUM	Clinical Dementia Rating Scale–Sum of Boxes
MCI	mild cognitive impairment
MMSE	Mini-Mental State Examination
NACC	National Alzheimer's Coordinating Center.

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TABLE 1

Baseline Demographic Information and Global Function in Patients Who Maintained a Diagnosis of Mild Cognitive Impairment (MCI) for 3 Years Versus Patients Who Converted from MCI to Dementia Within 3 Years

	Total (N = 1059)		Stable (N = 596)		Conversion (N = 463)		Effect Size [‡]	
	M	(SD)	M	(SD)	M	(SD)	P	d
Age (years)	74.37	(8.73)	73.68	(8.67)	75.27	(8.73)	0.003	0.18
Education (years)	15.17	(3.30)	14.93	(3.46)	15.48	(3.07)	0.007	0.18
Vascular burden	1.67	(1.40)	1.73	(1.41)	1.60	(1.40)	0.133	0.09
Global function								
Functional Activities Questionnaire	3.51	(4.66)	2.31	(3.71)	5.04	(5.26)	<0.001	0.61
Clinical Dementia Rating Scale–Sum of Boxes	1.48	(1.18)	1.09	(0.91)	1.97	(1.29)	<0.001	0.80
Mini-Mental State Examination [*]	–1.12	(1.94)	–0.61	(1.73)	–1.78	(2.00)	<0.001	0.63
	N	(%)	N	(%)	N	(%)	P	r
Sex								
Men	556	(52.50)	310	(52.01)	256	(53.13)	0.130	
Women	503	(47.50)	286	(47.99)	217	(46.87)		
<i>ApoE4</i> alleles [‡]							<0.001	0.20
0 copies	459	(43.34)	297	(49.83)	162	(34.99)		
1 copy	317	(29.93)	164	(27.52)	153	(33.05)		
2 copies	82	(7.74)	27	(4.53)	55	(11.88)		
Ethnicity [‡]							0.028	0.07
Non-Hispanic	1004	(94.81)	557	(93.46)	447	(96.54)		
Hispanic	54	(5.10)	38	(6.38)	16	(3.46)		
Mild cognitive impairment subtype							<0.001	0.16
Amnesic	893	(84.32)	475	(79.70)	418	(90.28)		
Nonamnesic	166	(15.68)	121	(21.30)	45	(9.72)		
Depression							0.020	0.06
None	731	(69.35)	427	(72.13)	304	(65.80)		

	Total (N = 1059)		Stable (N = 596)		Conversion (N = 463)		Effect Size [‡]	
	M	(SD)	M	(SD)	M	(SD)	P	d
Recent/active	323	(30.65)	165	(27.87)	158	(34.20)		
Diagnosis							0.065	
Clinician	145	(13.69)	71	(11.91)	74	(15.98)		
Consensus	914	(86.31)	525	(88.09)	389	(84.02)		

For details on the neuropsychological tests, see Weintraub et al. 2009.

* Shown as standardized z-score.

[†] Data were not available for *ApoE4* in 201 participants and ethnicity in 1 participant.

[‡] For the Cohen's *d*, effect sizes of 0.20, 0.50, and 0.80 indicate small, moderate, and large effects, respectively (Cohen, 1988). For *r* (categorical variables), the values are 0.10, 0.30, and 0.50, respectively (Cohen, 1988).

M = mean. **SD** = standard deviation. ***ApoE4*** = apolipoprotein E4 allele.

TABLE 2
Baseline Neuropsychological Test Scores for Groups with Mild Cognitive Impairment, Expressed as *z*-Scores

	Total (N = 1059)		Stable (N = 596)		Conversion (N = 463)		<i>P</i>	<i>d</i>
	<i>M</i>	(<i>SD</i>)	<i>M</i>	(<i>SD</i>)	<i>M</i>	(<i>SD</i>)		
Logical Memory Immediate Recall	−0.94	(1.17)	−0.61	(1.10)	−1.78	(2.00)	<0.001	0.69
Logical Memory Delayed Recall	−1.12	(1.19)	−0.74	(1.10)	−1.63	(1.13)	<0.001	0.80
Digit Span Forward	−0.40	(1.04)	−0.39	(1.05)	−0.41	(1.04)	0.845	0.01
Digit Span Backward	−0.33	(0.98)	−0.29	(0.98)	−0.38	(0.98)	0.179	0.09
Animal Fluency	−0.74	(0.90)	−0.58	(0.87)	−0.95	(0.89)	<0.001	0.42
Vegetable Fluency	−0.10	(1.12)	−0.11	(1.10)	−0.35	(1.08)	<0.001	0.42
Trail Making Test, Part A	−0.75	(1.62)	−0.63	(1.56)	−0.90	(1.68)	0.009	0.17
Trail Making Test, Part B	−1.06	(1.59)	−0.85	(1.47)	−1.33	(1.70)	<0.001	0.31
Digit Symbol	−0.50	(1.04)	−0.34	(1.02)	−0.71	(1.02)	<0.001	0.37
Boston Naming Test	−1.01	(1.55)	−0.89	(1.47)	−1.17	(1.62)	0.003	0.19

For details on the neuropsychological tests, see Weintraub et al, 2009.

* Effect sizes of 0.20, 0.50, and 0.80 indicate small, moderate, and large effects, respectively (Cohen, 1988).

M = mean. *SD* = standard deviation.

Table 3
Stepwise Logistic Regression Models Predicting Diagnostic Stability of Mild Cognitive Impairment (MCI)

Domain-Level Regression Models	Odds Ratio	(95% Confidence Interval)	P	Hosmer-Lemeshow P*	Area Under the Curve†
Demographic factors					
<i>ApoE4</i> alleles			< 0.001		0.67
0 versus 2	4.03	(2.38, 6.82)			
0 versus 1	1.84	(1.37, 2.39)			
Age (years)	0.96	(0.94, 0.98)	< 0.001		
Nonamnestic MCI subtype	1.84	(1.21, 2.80)	0.003		
No depression	1.63	(1.19, 2.24)	0.005		
Education (years)	0.96	(0.91, 1.00)	0.012		
Global function					
				0.40	0.76
Clinical Dementia Rating Scale—Sum of Boxes	0.57	(0.49, 0.67)	< 0.001		
Mini-Mental State Examination	1.32	(1.22, 1.42)	< 0.001		
Functional Activities Questionnaire	0.95	(0.91, 0.98)	< 0.01		
Neuropsychological performance					
				0.18	0.75
Logical Memory Delayed Recall	1.20	(1.15, 1.24)	< 0.001		
Vegetable fluency	1.11	(1.06, 1.16)	< 0.001		
Digit Symbol	1.04	(1.02, 1.05)	< 0.001		
Overall regression model					
				0.32	0.80
Logical Memory Delayed Recall	1.69	(1.43, 1.99)	< 0.001		
Clinical Dementia Rating Scale—Sum of Boxes	0.54	(0.46, 0.64)	< 0.001		
Mini-Mental State Examination	1.16	(1.05, 1.28)	< 0.001		
Age (years)	0.95	(0.93, 0.98)	< 0.01		
<i>ApoE4</i> alleles			< 0.01		
0 versus 2	2.83	(1.52, 5.26)			
0 versus 1	1.82	(1.48, 3.37)			
Digit Symbol	1.30	(1.09, 1.56)	< 0.01		

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For details on the neuropsychological tests, see Weintraub et al, 2009.

* Values > 0.05 indicate sufficient model fit (Tabachnik and Fidell, 1996).

[†] Values of 0.50 and 1.00 indicate poor and perfect prediction, respectively (Tabachnik and Fidell, 1996).

ApoE4 = apolipoprotein E4.